ORIGINAL ARTICLE

Antihypertensive drug prescription patterns, rationality, and adherence to Joint National Committee-7 hypertension treatment guidelines among Indian postmenopausal women

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ABSTRACT

Aim of Study: The aim of this study is to evaluate antihypertensive drug prescription patterns, rationality and adherence to Joint National Committee (JNC-7) hypertension (HT) treatment recommendations among Indian postmenopausal women (PMW).

Materials and Methods: An observational and cross-sectional prospective prescription audit study was carried over a period of 1 year. A total of 500 prescriptions prescribed to PMW for diagnosed HT, were identified for one point analysis. Drug prescription patterns/trends, and their adherence to JNC-7 report as well as rationality using WHO guide to good prescribing was assessed.

Results: In the monotherapy, category angiotensin receptor blockers (ARBs) accounted (24.8%), calcium channel blockers (CCBs) (19.4%), angiotensin converting enzyme inhibitors (ACEIs) (11%), beta blockers (BBs) (2.8%), and diuretics (2%) of the total prescription. Individually, amlodipine was maximally prescribed in 16.4%. 31.6% had double combination, whereas 2.2% and 1% had triple and four drug combinations, respectively. About 3.6% of the prescription contained antihypertensive combination along with other class of drug. ARBs + diuretic were observed in 11%, CCBs + BB 10% and ACEI + diuretic in 2.6% of the total prescriptions. Among the combination therapy amlodipine + atenolol (8.4%), telmisartan + hydrochlorothiazide (6%) and losartan + hydrochlorothiazide (4.4%) were maximally prescribed. 84.21% (P < 0.001) of the prescription showed nonadherence as per recommendations for pre-HT. 100% and 43.25% adherence rates were noticed for Stage 1 HT (P < 0.001) and Stage 2 HT (P > 0.05) patients.

Conclusion: Antihypertensive prescription trends largely adhere to existing guidelines and are rational except polypharmacy, generic and fixed dose combinations prescribing, were some of the common pharmacologically considered irrationality noticed.

Key Words: Elderly, hypertension, Joint National Committee-7, prescription trends, postmenopausal women, rationality

INTRODUCTION

The global burden of hypertension (HT) is alarming. The prevalence of HT increases with advancing age. HT affects more men than women until 55 years of age, but thereafter, women supersedes men. This increase in prevalence of various cardiovascular diseases, particularly HT, after the menopause may be related to metabolic and hormonal changes.

Furthermore, drug prescription in menopause is complex and many factors such as polypharmacy, comorbid conditions, pharmacokinetic and pharmacodynamic variability, and noncompliance make this group a high risk as far drug safety is concerned. Although studies are

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available analyzing prescription trends about antiHT across various age groups from Western and Indian setup, but there is no single study available in the literature regarding prescription trends and rationality of antiHT drugs among Indian postmenopausal women (PMW).

Hence, the current study was carried to evaluate antihypertensive drug prescription patterns, rationality and adherence to Joint National Committee (JNC-7) HT treatment recommendations among Indian PMW.

MATERIALS AND METHODS

An observational and cross-sectional prospective prescription audit study was carried out over a period of 1 year in teaching care tertiary hospital of North India. A total of 500 prescriptions prescribed to PMW (with cessation of menstruation for 1 year) for diagnosed HT, were collected for one point analysis from a tertiary care teaching hospital, primary and secondary government health care centers of Jammu province. Antihypertensive drugs were categorized according to the seventh report of the JNC on prevention, detection, evaluation, and treatment of high blood pressure (JNC-7). Detail epidemiological profile, common menopausal symptoms, presence or absence of any comorbid conditions, antihypertensive drug prescription patterns/trends and their adherence to available clinical practice guidelines/recommendations issued under JNC-7 as well as rationality of these prescriptions were assessed using prevalidated WHO guide to good prescribing. Data regarding antiHT monotherapy, dual combination and triple combination were recorded. Evaluation for rational drug therapy by evaluating average number of drugs per prescription, fixed dose combination (FDC) prescription rate, prescription laying down importance of lifestyle management, prescription with defined antiHT goals, prescriptions with correct dose strength and dosage schedule were evaluated. Number of prescriptions mentioning duration of therapy, over prescribing, banned drug formulation, debated rationality combinations, generic, and brand names used was also worked out. The prescriptions were collected by an independent person by clicking the picture by mobile outside the medical outpatient department and interviewing the PMW without the knowledge of prescriber to avoid any bias after taking verbal consent and after due administrative and Institutional Ethics Committee permission vide Number IEC/Pharma/Research/9c/2012/2741 dated 01.11.2012.

Statistical analysis

The statistical analysis was carried out using SPSS Version 15 for windows. Data were expressed in n (%). Chi-square test was applied for some of the parameters to prove their statistical significance. P < 0.05 was considered to be significant.

RESULTS

Sociodemographic profile of the study population revealed the mean age at menopause to be 51.35 and mean age at which HT was first diagnosed to be 47.45 years. Mean ± standard deviation number of menopausal symptoms was 4.70 ± 1.76. Mean duration since menopause was 4.7 ± 0.9 years. 415 (83%) of the population illiterate and 355 (71%) were from rural set up. 175 (35%) had active, 48 (8%) hectic, and 285 (57%) had sedentary lifestyle. 365 (73%) were vegetarian, 55 (11%) nonvegetarian, and 30 (6%) mixed.

Fatigue, lack of energy (32%), cold hand and feet, rheumatic pain (18%), cold sweats, weight gain, irritability and nervousness (16%) and palpitation of heart, excitable/ anxiety (11%) each were the most common menopausal symptoms in the current study.

62.4%, 27.6%, 7.2%, and 2.8% of the total PMW had isolated HT, HT with one, two, and more than two comorbid conditions, respectively. Acid peptic disease (7.6%), obesity/overweight (7.2%), diabetes (6.4%), dyslipidemia (4.8%), and anxiety (4%) were the most common comorbid conditions in the study population.

About 3.8% had pre-HT, 59.6% had Stage 1 and 36% were classified as Stage 2 HT and two (0.4%) and one (0.2%) were hypertensive urgency and emergency, respectively as per JNC-7 classification.

In the monotherapy, category angiotensin receptor blockers (ARBs) accounted for 24.8% followed by, calcium channel blockers (CCBs) (19.4%), angiotensin converting enzyme inhibitors (ACEIs) (11%), beta-blockers (BB) (2.8%), and diuretics (2%) of the total prescription. ARBs were prescribed most whereas BBs and diuretics were least prescribed. However, individually amlodipine was maximally prescribed in 16.4% of cases. Amlodipine among CCBs, telmisartan (10.2%) and losartan (8%) among ARBs, ramipril (6.8%) and enalapril (3.4%) among ACEIs and atenolol (1.8) and metoprolol (0.8%) among BBs were found maximally prescribed in their respective category [Table 1].

About 31.6% prescription had double combination, whereas 2.2% had triple combination and 1% had four drug combinations of antihypertensive drugs. About 3.6% of the prescription contained antihypertensive combination along with other class of drug ARB + diuretic were seen in 11% followed by CCBs + BB (10%) and
ACEI + diuretic in 2.6% of the total prescriptions. Among the combination therapy amlodipine + atenolol (8.4%), telmisartan + hydrochlorothiazide (6%) and losartan + hydrochlorothiazide (4.4%) were found maximally prescribed in our study population. Amlodipine + hydrochlorothiazide + telmisartan (1.6%) and amlodipine + hydrochlorothiazide + telmisartan + metoprolol (1%) were the frequently prescribed triple and four drug combinations, respectively. There was a tendency noticed of prescribing newly introduced antihypertensive drugs and their combinations such as clindipine, benazepril, olmesartan, valsartan, irbesartan, nebivolol, carvedilol, candesartan + hydrochlorothiazide, irbesartan + hydrochlorothiazide, and valsartan + hydrochlorothiazide [Table 2].

About 84.21% with \( P < 0.001 \) of the prescription showed nonadherence as per recommendations for pre-HT patients. 100% adherence was noticed with the recommendations for Stage 1 HT. 43.25% was the adherence rate seen among Stage 2 HT (\( P > 0.5 \)) patients. 100% adherence rate among the patients of hypertensive emergency and urgency with the JNC-7 guidelines with \( P < 0.001 \) were noticed, respectively [Table 3].

Average number of drugs per prescription was 4.57. Prescription rate stressing versus not stressing the importance of lifestyle management was 0.8% versus 99.2% (\( P < 0.001 \)). Prescription rate with defined versus undefined antihypertensive goals were observed in 3.8% versus 96.2% (\( P < 0.001 \)). Dose strength and schedule mentioned versus not mentioned rates were observed in 54% versus 46% and 86% versus 14% of prescriptions with \( P > 0.5 \) and \( P < 0.001 \), respectively. No banned drug formulation was noticed in any of the prescription. 3.6% of the total prescription were noticed with debated rationality pharmacologically in the form olmesartan + atorvastatin, amlodipine + atorvastatin and FDC in the form of five drug combination of aspirin + simvastatin + atenolol + ramipril + thiazide combination. Even tendency of prescribing combination with debated rationality sharing same group like telmisartan + ramipril and losartan + ramipril was noticed. FDC versus combination prescription rate was 91.04% versus 5.68% with \( P < 0.001 \) thereby indicating very high rate of FDC prescription. Similarly, maximum dugs were prescribed with their brand names. Generic name versus brand name prescription rate were 4.6% versus 95.4% (\( P < 0.001 \)) [Table 4].

**DISCUSSION**

The trends of anti-HT prescription are concerned in elderly population; the results of a recent Indian study carried by Mohd et al.[4] are in accordance to the current study. The most common drug classes prescribed in their study was CCBs 37% followed by angiotensin II receptor antagonists 21% and the most commonly prescribed drugs were amlodipine 37%, losartan 11%, and telmisartan 10%. Whereas, the most common antihypertensive FDC was telmisartan + hydrochlorothiazide 15% and most common two-drug combination was amlodipine + atenolol 7% followed by metoprolol + amlodipine 1%.

However, the results of current study were not fully in accordance to the study of Tiwari et al.[12] as far as drug prescription rate of BBs is concerned. They recorded 46.2% of prescriptions to have BBs, which is extremely high in comparison to our study which recorded only 2.8%. This might be due to the changing drug prescription trends as the study was of year 2004. Furthermore, fear of adverse drug reactions associated with BBs in elderly might be another reason for under prescribing of BBs. The role BB is more in

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**Table 1: Prescription pattern of antihypertensive mono-therapy**

| Antihypertensive | Total (%) |
|------------------|-----------|
| CCB             | 97 (19.4) |
| Amlodipine      | 82 (16.4) |
| Clindipine      | 1 (0.2)   |
| S-amlodipine    | 14 (2.8)  |
| ACEI            | 55 (11)   |
| Ramipril        | 34 (6.8)  |
| Lisinopril      | 2 (0.4)   |
| Enalapril       | 17 (3.4)  |
| Benazepril      | 2 (0.4)   |
| ARBs            | 124 (24.8)|
| Losartan        | 40 (8)    |
| Telmisartan     | 51 (10.2) |
| Olmesartan      | 18 (3.6)  |
| Valsartan       | 4 (0.8)   |
| Irbesartan      | 11 (2.2)  |
| Beta blocker    | 14 (2.8)  |
| Atenolol        | 6 (1.2)   |
| Metoprolol      | 4 (0.8)   |
| Nebivolol       | 2 (0.4)   |
| Carvedilol      | 2 (0.4)   |
| Diuretics       | 10 (2)    |
| Hydrochlorothiazide | 08 (1.6) |
| Chlorthalidone  | 0         |
| Indapamide      | 0         |
| Spironolactone  | 0         |
| Frusenamide     | 2 (0.4)   |
| Others:         | 3 (0.6)   |
| Total           | 303 (60.6)|

CCB: Calcium channel blocker, ACEI: Angiotensin converting enzyme inhibitor, ARBs: Angiotensin receptor blockers
HT with heart failure, acute coronary syndromes, and arrhythmias. The number of such patients was not very high in our study.

Calcium channel blockers (48.1%) and diuretics (1.9%) however showed[13] similar trends with the current study. ACE inhibitors (3.9%) and ARBs prescription rates in their study[17,18] was too low in comparison to our study. This might be because of recently gained popularity of ARBs and ACEIs. In combination therapy, a two-drug combination consisting of BBs and CCBs was given to the majority of the patients like our study.

Table 2: Prescription pattern of antihypertensive combination therapy

| Antihypertensive Combination FDC (%) | Total (%) | P value (Chi-square test) |
|--------------------------------------|-----------|--------------------------|
| Double combination                    | 158 (31.6)|                          |
| ACEI + diuretic                       |           |                          |
| Enalapril + hydrochlorothiazide       | 00        | 04 (0.8)                 | P < 0.001 |
| Ramipril + hydrochlorothiazide        | 00        | 08 (1.6)                 |            |
| Lisinopril + hydrochlorothiazide      | 00        | 01 (0.2)                 |            |
| ARB + diuretic                        |           |                          |
| Candesartan + hydrochlorothiazide     | 00        | 01 (0.2)                 | P < 0.001 |
| Irbesartan + hydrochlorothiazide      | 00        | 01 (0.2)                 |            |
| Losartan + hydrochlorothiazide        | 00        | 22 (4.4)                 |            |
| Olmesartan medoxomil + hydrochlorothiazide | 00        | 02 (0.4)                 |            |
| Telmisartan + hydrochlorothiazide     | 00        | 30 (6)                   |            |
| Valsartan + hydrochlorothiazide       | 00        | 01 (0.2)                 |            |
| BB + diuretic                         |           |                          |
| Metoprolol + hydrochlorothiazide      | 00        | 02 (0.4)                 | P > 0.05  |
| BB + ARBs                             |           |                          |
| Metoprolol + telmisartan              | 02 (0.4)  | 00                      | P > 0.05  |
| CCB + diuretic                        |           |                          |
| Amlodipine + hydrochlorothiazide      | 02 (0.4)  | 06 (1.2)                 | P > 0.05  |
| CCB + ARBs                            |           |                          |
| Telmisartan + amlodipine              | 3 (0.6)   | 9 (1.8)                  | P < 0.05  |
| Losartan + amlodipine                 | 1 (0.2)   | 7 (1.4)                  |            |
| CCB + ACEIs                           |           |                          |
| Amlodipine + lisinopril               | 00        | 4 (0.8)                  | P < 0.05  |
| CCB + beta blocker                    |           |                          |
| Amlodipine + atenolol                 | 6 (1.2)   | 36 (7.2)                 | P < 0.001 |
| Amlodipine + metoprolol               | 00        | 6 (1.2)                  |            |
| S-amlodipine 2.5 mg + atenolol 25 mg  | 00        | 2 (0.4)                  |            |
| ARBs + ACEIs                          |           |                          |
| Losartan + ramipril                   | 00        | 2 (0.4)                  | P > 0.05  |
| Telmisartan + ramipril                | 00        | 2 (0.4)                  |            |
| Triple combination                    |           | 11 (2.2)                 | P > 0.05  |
| Diuretic + ACE inhibitor + CCB        |           |                          |
| Amlodipine + lisinopril + hydrochlorothiazide | 00        | 1 (0.2)                  | P > 0.05  |
| Diuretic + BB + CCB                   |           |                          |
| Amlodipine + metoprolol + hydrochlorothiazide | 02 (0.4)  | 00                      | P > 0.05  |
| Diuretic + ARB + CCB                  |           |                          |
| Amlodipine + hydrochlorothiazide + telmisartan | 3 (0.6)   | 5 (1)                    | P > 0.05  |
| Four drug combination                 |           |                          |
| Amlodipine + hydrochlorothiazide + telmisartan + metoprolol | 5 (1)    | 00                      | P > 0.05  |
| Combination with other class of drugs |           |                          |
| Olmesartan + atorvastatin             | 00        | 4 (0.8)                  | P > 0.05  |
| Amlodipine + atorvastatin             | 00        | 8 (1.6)                  |            |
| Asprin + simvastatin + atenolol + ramipril + thiazide | 00        | 6 (1.2)                  |            |

JNC: Joint National Committee, CCB: Calcium channel blocker, ACEI: Angiotensin converting enzyme inhibitor, ARBs: Angiotensin receptor blockers, BB: Beta blocker, FDC: Fixed dose combination
Interestingly, in accordance to current study one study[12] showed under prescribed diuretics. The reasons may be patients inconvenience and increase likely hood of weakness, cramps, and electrolyte imbalance usually noticed with this group. JNC-8, expected in near future, may take the results of such studies into account and may redefine the status of such drugs like BB and diuretics.

The study of Dhanaraj et al[14] recorded highest prescription rates of ACE inhibitors (59%) followed by ARBs (52%), CCBs (29%), diuretics (27%), and BBs (14%). The results are unlike the current study as far as preference of ACEI over ARBs and BBs and diuretics are concerned. This may be because the study population in this study was HT with diabetes mellitus.

In another Indian study, BBs were the most frequently used group of drugs (46.7%), followed by calcium-channel antagonists (34.3%) and ACEIs (30%). Diuretics were used in only 13.2% of the prescriptions. Atenolol (36%), amlodipine (29.3%) and enalapril (19%) were the most frequently used individual drugs.[15]

Beta-adrenoceptor-blocking agents (51%), calcium antagonists (47%), and ACEIs (46%) were the most popular drugs. The utilization of thiazides was less than expected as documented in our study. Combination therapy was used more commonly than monotherapy (53.8% vs. 46.7%) unlike our study.[13]

Calcium channel blockers were the most preferred agents used, either as monotherapy or combination therapy in hypertensive patients with or without comorbidities in accordance to our study.[16]

Whereas, angiotensin II antagonists were in concurrence, while thiazides unlike our study were the most commonly used drugs in a study from Norway.[17]
The frequencies of using antihypertensive medicine\(^{(18)}\) among elderly population were CCB (64.15%), ACEIs (32.77%), diuretics (26.33%), BB (25.77%), ARB (23.81%), and alpha-blocker 4.20%, respectively. 42.86% were treated with monotherapy, while 57.14% with combined therapy. Among the combination therapy groups, the diuretic-based multiple therapy occupied 16.53%, and the nondiuretic-based multiple therapy held 40.62% like our study.

Adherence rates to JNC-7 were adequate in Stage 1, hypertensive emergency and urgency and inadequate in case of pre-HT and Stage 2 HT. Diuretics and BBs were under prescribed. This may be a reflection of drug prescription in elderly PMW, prescribing preference, patient related factors, and changing trends of antiHT prescription.

Polypharmacy, generic and FDC prescribing, prescribing of pharmacologically debated rationality antihypertensive combinations and newer drugs, not stressing on lifestyle management, were some of the common irrationality noticed in our study. Hence, the current study stress upon the need to optimize strategies to improve prescribing of medicines in elderly PMW.

Limitations of this study are that it was carried specially in PMW and trends were not compared with general population. The study was one point study and no follow-up was carried. No correlation of drug prescription with menopausal parameters was carried in the current study. Even it was beyond the scope the current study to assess’ rationality in term of comorbidity condition and antiHT prescription.

CONCLUSION

Amlodipine, telmisartan, losartan as monotherapy while amlodipine + atenolol and telmisartan + hydrochlorothiazide were maximally prescribed combinations. Adherence rates to JNC-7 were adequate in Stage 1, hypertensive emergency and urgency and inadequate in case of pre-HT and Stage 2 HT. Diuretics and BBs were under prescribed. Polypharmacy, generic and FDC, debated rationality antiHT combinations prescribing, were some of the common pharmacologically considered irrationality noticed in our study.

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