

Study of Prescribing Pattern and Adverse Drug Reactions in Hypertensive Patients with Comorbidities as per JNC 8 Hypertension Guidelines in a Tertiary Care Hospital of Punjab

Parminder Singh¹, Rahat Kumar Sharma², Jaswinder Singh³

¹Assistant Professor, Department of General Medicine, Sri Guru Ram Das Institute of Medical Sciences and Research, Punjab. ²Professor, Department of Pharmacology, Sri Guru Ram Das Institute of Medical Sciences and Research, Punjab. ³Professor, Department of Pharmacology, Sri Guru Ram Das Institute of Medical Sciences and Research, Punjab.

ABSTRACT

BACKGROUND

Adverse Drug Reactions (ADRs) to treatment in patients having hypertension with comorbidities is common; however, information about their incidence, severity and is scanty. Such patients are generally prescribed with multiple medications representing different calls of antihypertensive agents to control the blood pressure. Joint National Committee (JNC 8) has published the guidelines on the basis of evidence-based literature for the management of high BP in adults. This study was planned to study the ADRs associated with the drug-treatments prescribed as per JNC-8 guidelines in such patients.

METHODS

This study was conducted among patients prescribed with antihypertensive agents in medical OPD of SGRDIMS&R, Amritsar which is a tertiary care teaching hospital in Punjab. The study period was February 2019 - January 2020 i.e. for a period of one year. A total of 167 ADRs were detected, documented, assessed, and reported during the study period. Assessment of the ADRs revealed that diabetes mellitus is the most common association comorbidity in patients having hypertension and comorbidity.

RESULTS

The most common type of ADR was seen in prescribed four drug combination followed by three drugs and one drug prescribed. Two drug combination was the most suitable for such patients and among these, CCB + ACEI and CCB + ARB were the most tolerated in such cases. Causality assessment revealed that 27.5% of ADRs were possibly drug-related and 70.6% were mild in nature. Preventability of ADRs was assessed and it revealed that 74% of ADRs was preventable.

CONCLUSIONS

Drug combination of two drugs was best tolerated in such patients and such patients should be evaluated for comorbidities before prescribing drug treatment.

KEYWORDS

Adverse Drug Reactions, Hypertension, Comorbidity, JNC 8 Hypertension Guidelines

Corresponding Author:

*Dr. Parminder Singh,
Flat No-2, C2 Block,
Sri Guru Ram Das Institute of Medical
Sciences and Research, Mehta Road,
Vallah, Amritsar- 143006, Punjab.
E-mail: docpammy9732@gmail.com*

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BACKGROUND

WHO defines pharmacovigilance as "the pharmacological science relating to the detection, assessment, understanding and prevention of adverse effects, particularly long term and short term side effects of medicines".^{1,2} Hypertension is a common problem in India with prevalence of 25% urban and 10% in rural areas with a risk of cardiovascular (CV) disease in a linear fashion as with every increase of 20 mm Hg in SBP and/or increase of 10 mm Hg in DBP and doubling of risk of death from stroke, heart disease, or other vascular disease occurs.^{3,4} The first Joint National Committee (JNC) published the first hypertension management guidelines in the 1970s which were made primarily as an expert opinion of clinicians.⁵ In 1997, the Seventh Report of the JNC⁶ has simplified the classification of blood-pressure levels for hypertension prevention and management as Normal: SBP <120 and DBP <80, Prehypertension: SBP= 120-139 or DBP = 80-89, Stage 1 hypertension: SBP = 140-159 or DBP = 90-99 and Stage 2 hypertension: SBP ≥160 or DBP ≥100. The Committee concluded that thiazide diuretics either alone or in combination with other agents are recommended as initial therapy for uncomplicated hypertension.

In 2014, JNC 8 published the guidelines on the basis of evidence-based literature, systematic review and clinical trials for the management of high BP. These recommendations are that in patient aged ≥60 years, pharmacologic treatment may be started to lower systolic BP (SBP) ≥150 mm Hg or diastolic BP (DBP) ≥90 mm Hg.⁷ A revision of JNC-8 was done in 2017 and the guidelines were prepared regarding importance of ambulatory BP monitoring (ABPM), home BP monitoring (HBPM), BP thresholds needing antihypertensive drug treatment⁸ JNC-8 recommends that all persons 18 years (and those younger or older than 60 years with either diabetes or CKD) always initiate pharmacologic treatment with a target to lower SBP ≥140 or DBP ≥90 mm Hg. In India hypertension is responsible for 57% of all stroke deaths and 24% of all IHD deaths in India.⁹

According to Directorate General of Health Services (DGHS), Ministry of Health and Family Welfare, Government of India, the overall prevalence of hypertension in India by 2020 will be 159.46/1000 population.¹⁰ While treating hypertension, evidence suggests that reduction of the blood pressure by 5-6 mmHg can decrease the life time risk of stroke by 40%, of CAD by 15-20%, and also risk of dementia, heart failure. Among the recommended and most widely used antihypertensive drugs are the diuretics, angiotensin converting enzyme (ACE) inhibitors, calcium channel blockers (CCBs), beta adrenergic receptor blockers, and the angiotensin II receptor antagonists (ARBs).¹¹ Several studies^{12,13,14} had been carried out on ADRs related to antihypertensive drugs and the results has demonstrated high frequency of ADRs to antihypertensive treatment leading to the discontinuation of treatment. Monitoring of prescriptions and drug utilization studies could identify the associated problems and provide feedback to prescriber. ADR to antihypertensive agents in patients having

hypertension with comorbidities is common in clinical practice; however exact incidence is not known in Indian setup. So, this study was conducted to document, assess and report ADRs to antihypertensive drugs in a tertiary care teaching hospital of Punjab, India.

Primary Objectives

1. To identify drug prescribing pattern among hypertensive patients with comorbidities.
2. To assess the incidence of ADRs in hypertensive patients with comorbidities.

Secondary Objectives

1. To observe the demographic pattern of hypertensive patients with comorbidities.
2. To assess causality, severity and preventability of offending antihypertensive drugs.

METHODS

A prospective, observational study was conducted by Department of Medicine and Pharmacology in Sri Guru Ram das Institute of Medical Sciences & Research, Amritsar. The study was conducted from February 2019 till January 2020 i.e. for a period of one years. Approval from Institutional Ethics Committee was taken. The diagnosis and treatment was decided by the physician attending the patients in Department of Medicine. The patients having hypertension with comorbidities were included in the study and were given treatment for the disease as per JNC 8 guidelines. Patients were divided in Four groups on the basis of antihypertensive drug treatment as Group I: Patient taking single drug, Group II: Patient taking two drugs drug, Group III: Patient taking three drugs Group IV: Patient taking four drugs for the control of hypertension. Patients were allowed to take the treatment for the comorbid illness except any drug having interaction with the antihypertensive drugs prescribed. Identity of patient was kept as confidential. Monitoring and reporting of ADRs was done by either personal meeting / telephonic reporting to the Dept. of Medicine on 'CDSO ADR Reporting Form'.¹⁵ Patients were enrolled as per the inclusion criteria after taking informed consent.

Inclusion Criteria

1. Patients of both sexes diagnosed with hypertension having comorbidities like Diabetes Mellitus, CKD, Rheumatoid arthritis etc.
2. Patients requiring medical treatment on OPD basis.

Exclusion Criteria

1. Patients who required admission as having hypertensive emergency & hypertensive urgency.

2. Patient with History of recent attack (within 3 months) of acute myocardial infarction, acute left ventricular failure, acute stroke etc.
3. Pregnant women and lactating mother who were diagnosed with hypertension

RESULTS

The age and sex wise distribution of the patients having hypertension with comorbidities suggests that out of the total 114 hypertensive patients with comorbidities included in the study, 71 (62.2%) were male while 43 (37.7%) were female, indicating the higher prevalence of hypertension with comorbidities in male than in female population. Amongst males and females the hypertension with comorbidities was seen maximally in age group of >35-65 years as 41 (57.7%) and 32 (74.4%) respectively with a percentage of 64% of both males and females in the same age group. The most common comorbidity seen was diabetes mellitus (39.4%) followed by GI problem (24%), osteoarthritis (22.8%), IHD (21.9%), COPD (19.2%), CVA (14%) and from 1-10% having CKD, MI, Rheumatoid arthritis, Accidents, infection, CHF and others as shown in Table I. The other findings of the study is presented as-

Prescription Pattern of Antihypertensive Drugs Prescribed (Table II)

In the present study, 32 patients (28%) received monotherapy (Group I), 62 patients (54.3%) received two drugs (Group II), 16 (14%) received three drugs (Group III) and 04 (3%) patients received four drugs (Group IV) to control hypertension. Among the Group I, the various hypertensive classes prescribed were CCB's (34%) followed by ARB's (21%), ACEI (15%), BB (12.5%), AB (6%), D (6%) and CA (3%) respectively. In Group II, the most commonly prescribed drugs as fixed dose combination (FDC) or individually were CCB + ACEI (35.4%), CCB + ARB (22.5%), ARB + D (16.1%), ACEI + D (12.9%), CCB + BB (6%), BB + ARB (3%) and BB + D (1%) and BB + ARB (1%) respectively. In Group III, the most commonly prescribed drugs were CCB + B + D (18.7%), CCB + ACEI + D (18.7%), CCB + ARB + D (18.7%), ACEI + BB + D (12.5%) and (6%) for CCB + BB + CA, ARB + BB + D, AB + BB + D and AB + ACEI + BB and AB + ARB + BB respectively. In Group IV, the most commonly prescribed drugs were D + CCB + ACEI + BB (50%), D + CCB + ARB + BB (25%), D + CCB + AB + BB (25%) and nil for the other combinations used in the four drugs group as seen in our study respectively. ADRs reported in each group (Table III): Out of 167 ADRs reported, ADRs reported in each group was as 31 (18.5%) in group I, 26 (15.5%) in group II, 76(45.5%) in group III and 34 (20.3%) in group IV. In group I, ADRs associated with each drug was as CA (22%), D (22%), AB (19.3%), BB (16.1%) and 6% for CCB, ACEI, ARB.

This showed that in group I, CA and D has higher tendency to produce ADRs than other drugs and CCB, ACEI, ARB has least tendency for ADRs. In group II, ADRs associated with combination was higher in patients taking BB + ACEI (19.2%) and with CCB + BB, BB + ARB (15.3%) and was least (3%) with CCB + ARB, CCB + ACEI. In group III patients taking AB + ACEI + BB has 13.1% ADRs followed by AB + ARB + BB, CCB + CA + BB (11.8%) and only 7% with ACEI + BB + D, CCB + ARB + D and ARB + BB + D. Similarly, in group IV, 32.3% ADRs were seen in patients given D + CCB + ARB + AB, 38.2% in D + CCB + ARB + BB and lesser 29.4% with D + CCB + BB + ACEI.

Comorbidity	No. of Patients	%
CVA	14	12.2%
COPD	22	19.2%
DM	45	39.4%
IHD	25	21.9%
CKD	04	3%
MI	02	1%
CCF	06	5%
Liver Disease	02	1%
Asthma	08	7%
GI Problems	28	24%
Cancer	02	1%
Infection	01	1.6%
Osteoarthritis	26	22.8%
Rheumatoid Arthritis	04	3%
SLE	01	0.8%
Inflammatory Bowel Disease	01	0.8%
Renal calculi	01	0.8%
Others	09	7%

Table 1. Comorbidities of the Patients with Hypertension with Comorbidity

Group I N= 32	Group II N = 62	Group III N = 16	Group IV N = 04
CCB 11(9%)	ACEI + D	08(7%)	B + CCB + D 3(2%)
ACEI 5(4%)	ARB + D	10(8%)	ARB + CCB + D 3(2%)
ARB 7(6%)	CCB + ACEI	22(19.2%)	ARB + CCB + D 3(2%)
D 2(1.7%)	CCB + ARB	14(12.2%)	BB + CCB + CA 1(0.8%)
CA 1(0.8%)	CCB + BB	4(3%)	ARB + BB + D 1(0.8%)
BB 4(3%)	BB + D	1(0.8%)	ACEI + BB + D 2(1.7%)
AB 2(1.7%)	BB + ACEI	1(0.8%)	AB + BB + D 1(0.8%)
	BB + ARB	2(1.7%)	AB + ACEI + BB 1(0.8%)
			AB + ARB + BB 1(0.8%)

Table 2. Prescription Pattern of Antihypertensive Drugs in Patients with Hypertension with Comorbidity

ADRs Classification According to the System

ADRs were classified according to the system associated with the drugs given. The most common ADRs reported were of nonspecific nature (21.5%) as fatigue, restlessness, and uneasy feelings. The other ADRs related to systems were Nervous system (20.3%), Swelling (19.1%), gastrointestinal disturbances (14.3%), cardiovascular

Group I N= 31 (18.5%)	No. of ADRs (%)	Group II N = 26 (15.5%)	No. of ADRs (%)	Group III N = 76 (45.5%)	No. of ADRs (%)	Group IV N = 34(20.3%)	No. of ADR (%)
CCB	2 (6%)	ACEI + D	3 (11.5%)	B + CCB + D	11 (14.4%)	ARB + CA + CCB + D	Nil
ACEI	2 (6%)	ARB + D	3 (11.5%)	ACEI + CCB + D	9 (11.8%)	ARB + AB + CCB + D	11 (32.3%)
ARB	2 (6%)	CCB + ACEI	1 (3%)	ARB + CCB + D	6 (7%)	+ ARB + BB + CCB + D	13 (38.2%)
D	7 (22%)	CCB + ARB	1 (3%)	BB + CCB + CA	9 (11.8%)	ARB + CA + CCB + D	Nil
CA	7 (22%)	CCB + BB	4 (15.3%)	ARB + BB + D	7 (9%)	+ BB + CCB + CA + D	Nil
BB	5 (16.1%)	BB + D	5 (19.2%)	ACEI + BB + D	7 (9%)	ARB + CA + CCB + D	Nil
AB	6 (19.3%)	BB + ACEI	5 (19.2%)	AB + BB + D	8 (10%)	ARB + BB + CCB + D	10 (29.4%)
		BB + ARB	4 (15.3%)	AB + ACEI + BB	10 (13.1%)		
				AB + ARB + BB	9 (11.8%)		

Table 3. Drug Treatment and ADRs Reported (n=167) in Patients of Hypertension with Comorbidity

Sr. No.	System Organ Class	No. of ADRs Total (%)	Symptom Presented	Drug Category Responsible
1.	Nervous System	34 (20.3%)	Headache Dizziness Hypoesthesia Insomnia	CCB BB
2.	Respiratory System	11 (6%)	Depression Cough	ACEI
3.	Gastrointestinal Disorders	24 (14.3%)	Vomiting Diarrhoea Constipation Abdominal Pain	CCB Diuretics
4.	General	32 (19.1%)	Ankle edema Swelling of legs Fatigue	CCB
5.	Cardio-vascular system	12 (7%)	Palpitation Tachycardia Bradycardia Fall In BP	CCBs BB ACEI ARB
6.	Dermatological	09 (5%)	Rash Urticaria	ACEI ARB
7.	Metabolic disorder	09 (5%)	Hypokalemia Hyperkalemia Altered glucose metabolism	BB D ACEI ARB
8.	Non-Specific	36 (21.5%)	Fatigue Uneasy feeling Restlessness etc.,	All Drugs

Table 4. Classification of ADRs According to System and Drug Category Responsible (n= 167)

Disease	Age of Patient	Goal BP	Total Number of Patients (n=114)	
			Goal Achieved (No. /%)	Not Achieved (No. /%)
Without Diabetes or CKD (n= 26)	>60 years	<150/90	21 (18.4%)	4 (3%)
Without Diabetes or CKD (n= 73)	<60 years	<140/90	70 (61.4%)	6 (5%)
With Diabetes and without CKD (n= 12)	All Ages	<140/90	7 (6%)	2 (1%)
With diabetes and with CKD (n= 03)	All Ages	<140/90	3 (2%)	1 (0.8%)

Table 5. BP Goals as per JNC 8 Achieved in Patients of HT with Comorbidity

problems (7%), respiratory problems (6%) and (5%) in case of dermatological, metabolic disturbances.

WHO Causality and Hartwig and Siegel’s Severity Assessment Scale

On the WHO Causality and Hartwig and Siegel’s Severity Assessment Scale,¹⁶ 23% ADRs were classified as possible, 98% as probable and 46% as certain. On severity assessment scale i.e. modified Hartwig and Siegel’s scale,¹⁷ which classifies severity of ADR as mild, moderate and severe 70.6% were mild, 26.3% were moderate and only 2% were of severe type of ADRs. Assessment of Preventability of ADRs by Modified Schumock and Thornton Scale:¹⁸ The analysis of the data showed that out of 114 patients included in the study, 64.9% ADRs were of definitely preventable type and 28% and 12% were of probably and not preventable in nature.

Blood Pressure Goal in Patients of Hypertension with Comorbidity (Table 5)

The blood pressure goal achieved as per Joint National Committee (JNC 8) guidelines in patients having

hypertension with comorbidities was as 68% (with age <60 years and without diabetes or CKD), 22% (with age >60 years and without diabetes or CKD), 8% (all age and with diabetes or CKD) and 2% (all ages and with diabetes and CKD). Table V This showed that the blood pressure control was not adequately achieved in patients having both diabetes and CKD and patients having no diabetes or CKD with age <60 years had maximum achievement of blood pressure control.

DISCUSSION

HT is a chronic disease needing lifelong treatment and drugs use is unavoidable in many patients. This study analysed the prescription pattern in hypertensive patients with comorbidities attending the OPD in a tertiary care hospital attached to SGRDIMSAR, a tertiary care teaching hospital ADRs are an important consideration in the management of patients with hypertension as 50% of the patients who developed an ADRs discontinued their medicines.¹⁹ The demographic details of our study population showed male gender predominance over females, which was dissimilar to the reports of other studies.^{20,21} This might be due to higher

proportion of the comorbidities in male patients having hypertension.

A similar study conducted by Krishna Murti et al.²² showed that 35% of male belong to age group of 40-60 years and 12.4% of female. The most common morbidity with hypertension observed in our study was diabetes mellitus (39.4%) followed by GI problems (24%), osteoarthritis (22.8%), IHD (21.9%), COPD (19.2%) and from 12.2 to 0.8% for other diseases. (table I) This reason was probably due to rising incidence of obesity associated with its complications like hypertension, IHD, osteoarthritis. It was observed that in our study, that out of 114 patients prescribed antihypertensive drugs, 28% patients received monotherapy, while majority of the patient's i.e. 72% were given multidrug therapy. In multidrug therapy groups 54% patients were on two drug therapy, 14% of patients on three drug therapy and 03% on four drugs (table II).

Because hypertension is associated with various concurrent diseases, so polypharmacy is quite prevalent form of practice in such patients. The overall percentage of ADRs in our study was 18.5% in group I, 15.5% in group II, 45.5% in group III and 20.3% in group IV. This indicates that the percentage of ADRs was lowest in patients taking two drugs therapy. In the overall utilization pattern of antihypertensive agents in 114 patients, the most common monodrug therapy were CCB's (9%) followed by ABRs (6%), ACEI (4%), BB (3%) and less commonly used drug class was D, AB, CA class of drugs (Table II). In multidrug therapy the most common drug combination in two drug therapy was CCB + ACEI (19.2%), CCB + ARB (12.2%) followed by ARB + D (8%), ACEI + D (7%), and less commonly drug class used were CCB + BB, BB + ARB, BB + ACEI (1.7 to 0.8%). Similarly in three drugs combination the most common combination of drug group was 2% each for CCB + B + D, CCB + ACEI, CCB + ARB + D and followed by other drug combinations like ACEI + BB + D, CCB + CA + BB, ARB + BB + D, AB + BB + D, AB + ACEI + BB and AB + ARB + BB from 1.7% to 0.8% respectively. In four drug class combination, 1.7% received D + CCB + ACEI + BB followed by 0.8% for D + CCB + BB + AB, D + ARB + CCB + BB and nil for the other drug class combinations (Table II). Krishna Murti et al.²² observed that of 137 patients, 27.7% patients were received monotherapy and multidrug therapy in 72.2% patients. In multidrug therapy, 68.6% patients were on two drugs, 27.2% patients on three drugs and 4.0% on four drugs. Sandozi and Emani²³ observed that ACE inhibitor was the most commonly prescribed drug (79.6%) followed by BB (54.2%), CCB (33.8%), loop diuretic (17%).

This is in not consonance with our study as the most common drugs prescribed was CCB followed by ACEI, ARB, BB and diuretics. The difference might be due to individual choice of the physician prescribing treatment. The ADRs reported in each group as shown in Table III, indicates that patients in group III has highest rate of ADRs (45.5%) as compared to group IV (20.3%), group I (18.5%) and least in group II (15.5%). Similarly, Table III shows that ADRs incidence was highest in group IV prescribed D + CCB + ARB + BB (38.2%) followed by D + ARB + CCB + AB (32.3%), D

+ CCB + BB + ARB (29.4%) group IV and CCB + B + D (14.4%), AB + ACEI + BB (13.1%), AB + ARB + BB (11.8%) and in range of 6-10% with other drug combinations in group III. In group I, ADRs pattern was as 22% for CA, D, 19.3% for AB, 16.1% for BB and 6% for other drugs like CCB, ACEI, and ARBs. In group II, BB + D and BB + ACEI had 19.2% ADRs followed by 15.3% for BB + ARB and BB + D and 11.5% for ACEI + D and ARB + D and lowest i.e. 3% with CCB, ARB and ACEI. This clearly indicates that the fixed dose combination (FDC) or the drug combination of CCB with ACEI or ARB is best tolerated in patients having hypertension with comorbidities. The drug selection criteria is important while deciding the type of treatment to patients of HT with comorbidity. Older patients usually respond to CCB. Patients with DM, CKD, and heart failure usually require ACEIs. Many epidemiological studies have shown that patients of HT with comorbidity were given multiple therapies and so are more likely to develop ADRs^{24,25} QUADS,²⁶ reported CCB (65%) were the most commonly prescribed drugs followed by BB (64%) and ACEIs (33%).

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. In our study, we found CNS side effects were high followed by swelling, GI disorders, cardiovascular system, respiratory system, dermatological and metabolic disorders. (table V) Previous studies have advocated the same,²⁷ however Hussain et al¹³ reported cardiac ADRs are more common (35.3%) followed by GIT disorders (20.6%). While Alomar and Strauch²⁸ observed, headache followed by GIT, fatigue and numbness, dizziness and oedema related side effects. Different type of ADRs observed is due to different prescription pattern of antihypertensive drugs in the study. BP goal achieved according to JNC-8 guidelines in our study was as patients <60 years without diabetes or CKD 68% achieved the goal while only 22% with age >60 years achieved the goal. In patients with Diabetes and without CKD (all ages) 50% achieved the goal (<140/90 mmHg) and patients with CKD with or without DM (all ages), only 8% achieved the goal. Only 2% patients had control of blood pressure in patients having diabetes and CKD together.

Malpani et al,²⁹ observed patients without diabetes or CKD (>60 years), 75.60% achieved the goal and patients without diabetes or CKD (<60 years) 64.30% achieved the goal of BP<140/90 mmHg. Patients of all ages with Diabetes and without CKD, 50% achieved the goal (<140/90 mmHg) and patients with CKD with or without DM, 60% achieved the goal (<140/90 mmHg). These finding are not in concordance to our study where poor control of blood pressure was seen in patients having both diabetes and CKD and good control of blood pressure was seen in patients having no diabetes or CKD and age <60 years. In present study according to WHO causality assessment scale most of ADRs were "probable" (58.6%) followed by "possible" (27.5%) and "certain" (13.7%). Hussain et al¹² found most common ADRs were "possible" (47.1%), followed by "probable" (35.5%) and "certain" (2.9%). In our study most of ADRs were "probable" which suggest that these ADRs are

due to antihypertensive drugs and are unlikely to be attributed to concurrent disease or other drugs. According to Hartwig and Siegel severity assessment scale 70.6% ADRs were "mild" and 26.3% were "moderate" and 2% ADRs were severe whereas in Hussain et al¹² study, it was observed that 52.9% ADRs were "mild", 41.2% were "moderate" and 5.8% were "severe" Thus our findings are in concordance to the study of Hussain et al signifying that most of the ADRs were of mild type and require no treatment.

CONCLUSIONS

This study provided baseline details of the prescribing pattern of drugs in patients of hypertension with comorbidities. Since hypertension is a chronic disorder, a combination of various class of drugs is recommended for adequate control and to prevent future onset of complications. Thus the drug combination is prescribed which has minimum ADRs and have multisystemic benefits in such patients and this is one of the most important factors which affects adherence of the patients to treatment. Thus, the findings of this study is helpful in deciding the course of treatment in patients having hypertension with comorbidities.

Abbreviations

ADRs: Adverse Drug Reactions,
ACEI: Angiotensin Converting Enzyme Inhibitor;
AB: Alpha Blocker;
ARB: Angiotensin Receptor Blocker;
CCBs: Calcium Channel Blockers;
BBs: Beta Blockers;
CA: Centrally Acting Agent,
D: Diuretics.
ALD: Alcohol Liver Disease;
CAD: Coronary Artery Disease;
CCF: Congestive Cardiac Failure;
CVA: Cerebrovascular Accident;
COPD: Chronic Obstructive Pulmonary Disease;
CKD: Chronic Kidney Disease;
DM: Diabetes Mellitus;
HTN / HT: Hypertension;
IHD: Ischemic Disease;
LVF: Lower Ventricular Failure;
MI: Myocardial Infarction;
JNC: Joint National Committee;

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