

An Assessment of Antihypertensive Drug Utilization Patterns and Adherence to JNC-7 Guidelines in South Indian Tertiary Care Teaching Hospital

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ABSTRACT

Objective: The objective of this study was to assess the adherence of antihypertensive medication to Joint National Committee (JNC)-7 and drug-drug interactions between drugs prescribed for patients with hypertension and its co-morbidities in a south Indian tertiary care teaching hospital. **Methods:** A total of 200 hypertension prescriptions were collected in a prospective observational study from February 2014 to July 2014. Medication adherence was assessed by comparing with the JNC-7 guidelines and drug-drug interactions were reported after checking in standard databases for their mechanism of interaction. **Results:** The average age was 58.8 ± 2.40 years (males) and 53.7 ± 2.3 years (females). Stage 1 hypertension (36%, males; 35.2%, females) was most predominant than stage 2 hypertension (29.33%, males; 30.4%, females) and hypertension emergency (25.33%, males; 23.2%, females). Diabetes mellitus (19%, males; 45%, females) and cardiovascular diseases (27%, males; 36%, females) are the most common co-morbidities in hypertension patients followed by renal diseases. Calcium channel blockers (9.4%) are most widely prescribed drugs followed by angiotensin receptor blockers (6.9%) and diuretics (6.9%) in monotherapy. Angiotensin receptor blocker + diuretic combination (4.9%) was mostly used in two drug combination therapy. The overall rate of adherence was 15.6% (Pre hypertension); 37.87% (Stage 1 hypertension); 26.21% (Stage 2 hypertension) and 50% (Hypertension emergency). In the present study, the major drug interaction was digoxin and angiotensin receptor blockers (11.9%) followed by the clopidogrel + calcium channel blockers combination (9.5%). **Conclusion:** Results reveal that optimal medication adherence to JNC-7 guidelines was not observed in the prescriptions.

Key words: Hypertension, Joint National Committee (JNC), Medication adherence, Drug-Drug interactions, Stroke.

INTRODUCTION

Hypertension is the most common disorder affecting the heart and blood vessels. Approximately 7.6 million deaths (13-15% of the total) and 92 million disability-adjusted life years worldwide were attributable to high blood pressure in 2001.¹ It is predominantly an asymptomatic condition and in more than 95% of cases, a specific underlying cause of hypertension cannot be found.² Many risk factors may contribute to its development, including age, gender, weight, physical activity, smoking, family history, serum cholesterol, diabetes mellitus, renal dysfunction, peripheral resistance vessel tone, endothelial dysfunction, autonomic tone, insulin resistance and neurohumoral

factors. Hypertension doubles the risk of cardiovascular diseases, including coronary heart disease (CHD), congestive heart failure (CHF), ischemic and hemorrhagic stroke, renal failure, and peripheral arterial disease if not effectively treated.^{3,4}

Until about 1950, there was no effective treatment, and the development of antihypertensive drugs has been a major therapeutic success story. Now, high blood pressure can be controlled through existing antihypertensive drug therapy by following some guidelines. The Joint National Committee (JNC-7) is considered the “gold standard” consensus guidelines for

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the management of hypertension. The other guidelines are 2007 American Hypertension Association (AHA) and the 2007 European Society of Hypertension/European Society of Cardiology.⁵⁻⁷ The overall principles common to these guidelines are to implement life style modifications in addition to pharmacotherapy to control BP in patients with hypertension. Patient's optimal adherence with antihypertensive drug therapy is essential for preventing serious complications with hypertension over the long term. Therefore the objective of this study was to evaluate the antihypertensive drug utilization pattern and drug-drug interactions between the drugs prescribed to hypertensive patients in a south Indian tertiary care teaching hospital.

METHODS

Experimental Design and Data collection procedure

A prospective observational study was conducted in a South Indian hospital, Andhra Pradesh and the protocol

was approved by the Institutional ethical committee of KVSRR Siddhartha College of Pharmaceutical Sciences. A total of 200 prescriptions were collected from hypertension patients. Each prescription includes the drug, quantity, duration, and date of dispensing. Each antihypertensive medication was categorized into one of the following classes: thiazide-type diuretics, angiotensin converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), calcium channel blockers (CCBs), β -blockers and other antihypertensive agents. Medication Adherence was assessed by comparing with JNC-7 treatment guidelines shown in Figure 1.

Statistical Analysis

Statistical differences were determined by using Graph pad (version 5.0, Chicago, USA) and SPSS 20 version. Patient characteristics and prescription details were compared using analysis of variance and χ^2 test for continuous and categorical variables, respectively. P values < 0.05 were considered statistically significant.

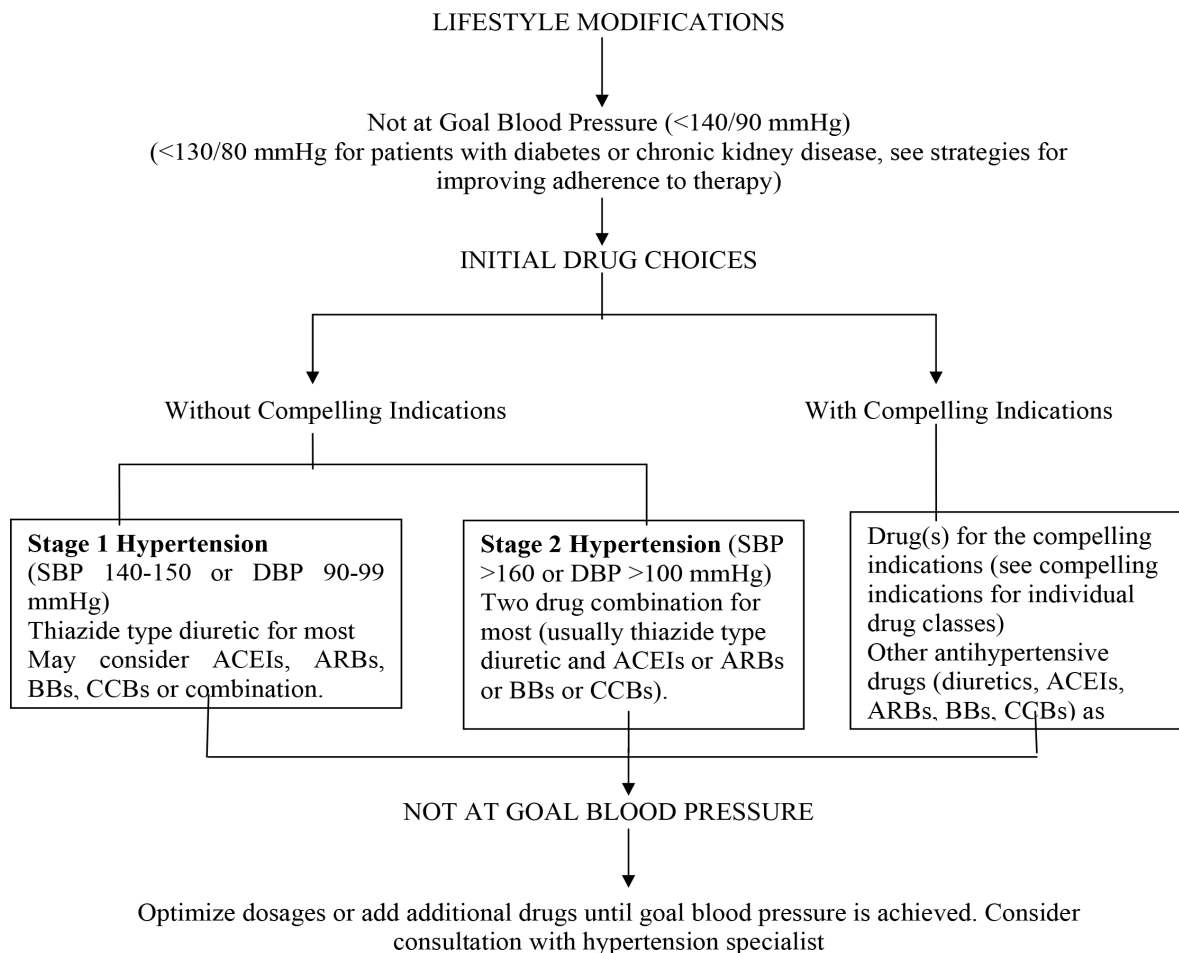


Figure 1: Algorithm for treatment of hypertension according to Joint National Committee (JNC-7).

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; ACEIs: Angiotensin converting enzyme inhibitors; ARBs: Angiotensin receptor blockers; BBs: β -blockers and CCBs: Calcium channel blockers.

Table 1. Baseline demographic and clinical characteristics of hypertension patients with associated co-morbidities (n=200)

	Males 75 (37.5%)	Females 125 (62.5%)	Test	P- Value
Age (Mean ± SD)	58.8 ± 2.40	53.7 ± 2.3	t-test	0.0001
<20, n (%)	0 (0)	0 (0)	-	-
20-39, n (%)	3 (4.0)	9 (7.2)	χ ²	0.468
40-59, n (%)	31 (41.33)	57 (45.6)	χ ²	0.746
>60, n (%)	41 (54.66)	59 (47.2)	χ ²	0.359
Systolic Blood Pressure (Mean ± SD)	154.5 ± 5.52	153.6 ± 5.03	t-test	0.239
Normal (<120 mmHg), n (%)	5 (6.66)	10 (8.0)	χ ²	0.917
Pre HTN (120-139 mmHg), n (%)	11 (14.66)	21 (16.8)	χ ²	1.00
Stage 1 HTN (140-159 mmHg), n (%)	27 (36.0)	39 (31.2)	χ ²	0.771
Stage 2 HTN (160-179 mmHg), n (%)	13 (17.33)	26 (20.8)	χ ²	1.00
HTN emergency (≥180 mmHg), n (%)	19 (25.33)	29 (23.2)	χ ²	0.766
Diastolic Blood Pressure (Mean ± SD)	105.15 ± 5.39	81.25 ± 4.69	t-test	0.0001
Normal (< 80 mmHg), n (%)	12 (16.0)	13 (10.4)	χ ²	0.501
Pre HTN (80-89 mmHg), n (%)	14 (18.66)	25 (20.0)	χ ²	0.435
Stage 1 HTN (90-99 mmHg), n (%)	21 (28.00)	44 (35.2)	χ ²	0.222
Stage 2 HTN (100-119 mmHg), n (%)	22 (29.33)	38 (30.4)	χ ²	0.343
HTN emergency (>120 mmHg), n (%)	6 (8.0)	5 (4.0)	χ ²	1.000
Co-morbid states				
Diabetes Mellitus (%)	19	45		
Cardio vascular diseases (%)	27	36		
Renal diseases (%)	5	10		
Liver Diseases (%)	10	3		
Hypothyroidism (%)	1	3		
Anemia (%)	2	2		
CNS (%)	3	5		
Lungs (%)	6	2		
Others (%)	17	4		
Number of drugs in a prescription, n (%)				
1-3		33 (16.5)		
4-6		132 (66)		
7-9		35 (17.5)		
>10		0 (0)		

SD, Standard deviation; HTN, Hypertension; CNS, Central nervous system.

RESULTS

Two hundred prescriptions were collected randomly in the duration of six months to assess medication adherence. The demographic and clinical characteristics were shown in Table 1. Total 125 (62.5%) females and 75 (37.5%) males were indentified. The mean age was 58.8 ± 2.40 years (males) and 53.7 ± 2.3 years (females). Hypertension was found to be significant in females when compared to males (Table 1). Hypertension was classified according to JNC-7 guidelines and found 17% (pre hypertension), 36% (stage 1 hypertension), 33 % (stage 2 hypertension) and 14% (hypertensive emergency) cases. The mean systolic blood pressure was 154.5 ± 5.52 mm Hg (males) and 153.6 ± 5.03 mm Hg (females). The mean diastolic blood pressure was 105.15 ± 5.39 mm Hg (males) and 81.25 ± 4.69 mm Hg (females). Stage 1 hypertension

(36%, males; 35.2%, females) was most predominant than stage 2 hypertension (29.33%, males; 30.4%, females) and hypertension emergency (25.33%, males; 23.2%, females). Diabetes mellitus (19%, males; 45%, females) and cardiovascular diseases (27%, males; 36%, females) are the most common co-morbidities in hypertension patients followed by renal diseases. The average number of drugs prescribed to each patient was 4-6 (66%).

Table 2 shows the mono and combination therapies for the treatment of hypertension. As per present study, most of the physicians prescribed single drug (monotherapy, 29.3%) to control BP followed by three-drug combination (12.7%) and two-drug combination (12.2%). Calcium channel blockers (9.4%) are most

Table 2: Antihypertensive medications used by hypertensive patients (males and females) in mono and combination therapies

Treatment	n (%)
Monotherapy	72 (29.3)
Calcium channel blockers	23 (9.4)
Angiotensin receptor blockers	17 (6.9)
Diuretics	17 (6.9)
β-blockers	9 (3.7)
ACE Inhibitors	6 (2.4)
Double Combination	30 (12.2)
Angiotensin receptor blockers + Diuretics	12 (4.9)
Calcium channel blockers + β-blockers	04 (1.6)
Diuretics + Calcium channel blockers	2 (0.8)
Diuretics + β-blockers	2 (0.8)
Calcium channel blockers + α-agonists	4 (1.6)
ACE inhibitors + Diuretics	2 (0.8)
Calcium channel blockers + Calcium channel blockers	2 (0.8)
ACE Inhibitors + ACE Inhibitors	2 (0.8)
Triple Combination	31 (12.7)
Calcium channel blockers + Angiotensin receptor blockers + Diuretics	18 (7.4)
Angiotensin receptor blockers + Diuretics + Diuretics	2 (0.8)
Calcium channel blockers + β-blockers + Diuretics	02 (0.8)
Diuretics + β-blockers + Calcium channel blockers	06 (2.4)
Angiotensin receptor blockers + Calcium channel blockers + β-blockers	3 (1.2)
Four Drug Combination	5 (2.0)
Diuretics + Calcium channel blockers + β-blockers	02 (0.8)
Angiotensin receptor blockers + Diuretics + Calcium channel blockers	03 (1.2)
Combination With Other Drugs	106 (43.4)

ACE, Angiotensin converting enzyme.

Table 3: Adherence to JNC-7 hypertension treatment recommendations

JNC-7 Hypertension Classification	Recommendations	Non adherence rate (%)	Adherence rate (%)	P-Value (Chi-Square Test)
Pre hypertension	No drug indicated	84.4	15.6	P<0.0001
	Thiazide type diuretics for most		37.87	
Stage 1 hypertension	For many consider	62.13	4.54	P<0.05
	ACEIs		12.1	
	ARBs		3.03	
	BBs		18.2	
	CCBs		26.21	
Stage 2 hypertension	2 Drug combinations for most (usually thiazide type)	73.71	0	P<0.0001
	ACEIs + Diuretics		14.75	
	ARBs + Diuretics		4.91	
	BBs + Diuretics		6.55	
	CCBs + Diuretics			
Hypertensive emergency	Nifedipine SL/furosemide i.v./ Metoprolol i.v.	50	50	P>0.05

ACEIs, Angiotensin converting enzyme inhibitors; ARBs, Angiotensin receptor blockers; BBs, β-blockers; CCBs, Calcium channel blockers.

widely prescribed drugs followed by angiotensin receptor blockers (6.9%) and diuretics (6.9%) in monotherapy. Angiotensin receptor blocker + diuretic combination (4.9%) was mostly used in two drug combination therapy followed by Calcium channel blocker + β-blocker combination. The overall rate of adherence was 15.6% (Pre hypertension); 37.87% (Stage 1 hypertension);

26.21% (Stage 2 hypertension) and 50% (Hypertension emergency) presented in Table 3.

DISCUSSION

Hypertension is a very common medical condition worldwide and is the principal cause of stroke, is a

major risk factor for coronary artery disease and its complications. It is a major contributor to cardiac failure, renal insufficiency, and dissecting aortic aneurysm. Choice of an antihypertensive drug should be driven by likely benefit in an individual patient, taking into account concomitant diseases such as diabetes mellitus, problematic adverse effects of specific drugs, and cost. The overall goal of treating hypertension is to reduce hypertension associated morbidity and mortality.^{1,8} The Seventh Report of the JNC on the Detection, Evaluation, and Treatment of High Blood Pressure is the most prominent evidence-based clinical guideline for the management of hypertension, supplemented by the 2007 American Heart Association (AHA) Scientific Statement on the treatment of hypertension. As per 2007 AHA guidelines, ACEIs, ARBs, CCBs, thiazide diuretic, or a two-drug combination are recommended for first-line therapy for primary prevention patients.⁶ This is in contrast to the JNC-7 guidelines that placed preference on using a thiazide diuretic over other agents for most patients, and also included a β -blocker as a potential first-line option followed by ACEIs, ARBs, CCBs, and thiazide diuretics shown in Figure 1.⁵ But the present study results revealed that the overall rate of adherence was 15.6% (Pre hypertension); 37.87% (Stage 1 hypertension); 26.21% (Stage 2 hypertension) and 50% (Hypertension emergency). Previous studies show that a simple evidence-based guideline appears to be effective in raising the quality of antihypertensive therapy in United States of America⁹ and China.¹⁰ Physicians in south Indian hospitals should follow the evidence based guidelines (JNC-7) to improve the patient care like America and China.

Drugs are often used in combination to achieve a preferred therapeutic goal or to treat coexisting diseases. Because of the risk related to concomitant use of drugs, co-medication has become a general concern and an important concept in term of prescribing appropriateness. Some combinations may result in undesired pharmacodynamic or pharmacokinetic interactions, resulting in undertreatment or harmful effects.^{11,12} The consequences of drug-drug interactions (DDIs) can range from no untoward effects at all, to drug-related mortality. Although DDIs are considered to be preventable, studies up to 11% of patients experience symptoms associated with DDIs,¹³ and DDIs are responsible for up to 2-3% of hospital admissions.^{14,15} DDIs are associated with increased health care use.^{16,17}

Although DDIs are one of the most significant problems with drug prescribing,¹⁸ most physicians are

not fully aware of all major and clinically important drug interactions,^{19,20} or underestimate the risk of the co-administration of multiple drugs.²¹ Furthermore, the pharmacist rarely intervenes when it recognizes the presence of a potentially clinically important DDI.^{22,23} Research using prescription databases can contribute to a better understanding of potential DDIs (pDDIs); however, only a few studies have examined clinically important DDIs in an outpatient setting, and even fewer have identified patients at risk.^{24,25} In the present study, a total of 42 interactions were found in the 200 prescriptions. The majority of prescriptions contained 4-6 (66%) drugs followed by 7-9 (17.5%). Drug interactions are classified into major and moderate after checking the data bases. The prevalence of major and moderate DDIs was 40.44% and 59.36% respectively. Afterwards, all drug interactions were classified by the research team into categories of clinical relevance (A-F) as well as categories of available evidence (0-4) according to the classification system and found that 63 (72.4%) 3D and 9 (10.3%) 3A interactions.

CONCLUSION

Our results reveals that antihypertensive medication adherence to JNC-7 guidelines is suboptimal. Therefore, physicians should follow JNC-7 guidelines to improve the patients care because suboptimal adherence leads to adverse clinical outcomes.

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CONFLICT OF INTEREST

The authors declare that this research does not have any conflict of interest with anyone or any Institute.

Key Points

- The overall rate of adherence to JNC7 guidelines was 15.6% with respect to the treatment of Pre hypertension.

- The overall rate of adherence to JNC7 guidelines was 37.87% with respect to the treatment of Stage 1 hypertension.
- The overall rate of adherence to JNC7 guidelines was 26.21% with respect to the treatment of Stage 2 hypertension.
- The overall rate of adherence to JNC7 guidelines was 50% with respect to the treatment of Hypertension emergency.

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