Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2016, 8(2):479-483

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Study of prescribing trends of anti-hypertensive drugs in a hospital at Jaipur

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ABSTRACT

The study evaluates prescribing pattern of antihypertensive drugs in patients of hypertension visiting hospital at Jaipur, Rajasthan. Prescriptions of hypertensive patients with or without comorbidities attending various outpatient departments were selected randomly. Prescriptions of pregnant women and children below 18 years of age were excluded. Patient's demographics, antihypertensive drugs prescribed and comorbid conditions were entered in a specially designed proforma. A total of 227 prescriptions were monitored of which 134 were males and 93 were females divided in 20-89 year age groups. Majority of hypertensive cases were in 50-59 years for males and 40-49 years for females. Of total, 67.84% were treated with dual therapy, 32.15% with monotherapy and only 12.33% were treated with multiple therapy. As monotherapy angiotensin receptor blockers (ARBs) were the most commonly (52.05%) prescribed of which losartan alone contributed (97.43%). In dual therapy, combination of losartan & hydrochlorthiazide was given to majority of patients of essential HTN. Diuretics despite being recommended as first line drug by JNC VII failed to be leading agent as monotherapy.

Keywords: Antihypertensive drugs, prescription pattern, blood pressure, drug utilization, combination therapy

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INTRODUCTION

Globally cardiovascular disease accounts for approximately 17 million deaths a year which is nearly one third of the total. According to World Health Report 2002, cardiovascular diseases (CVDs) will be the largest cause of death and disability by 2020 in India **[1]**. Hypertension (HTN) has emerged as an important contributor to global burden of cardiovascular morbidity and mortality **[2]**. It has been found to be the cause for 57% of all stroke deaths and 24% of all coronary heart disease (CHD) deaths**[3]**.In India prevalence of hypertension in year 2000 was 60.4 million males and 57.8 million females and is expected to rise to 107.3 million and 106.2 million respectively by 2025 **[4]**. It has been reported that 30% of men and 33% women suffer from HTN in urban areas of Jaipur, Rajasthan while in rural population prevalence has been observed to be low (men: 27%; women: 17%) **[5].** Further it has been reported that age and obesity has significant positive correlation with prevalence of hypertension in rural as well as urban population **[6].**Hypertension if not checked will have significant socio-economic impact as nearly 80% of CVD deaths occur in low and middle-income countries.

The physicians are supposed to achieve the goal blood pressure of a patient following recommendations and guidelines of JNC VII 2003 and JNC VIII 2013. This may be assessed by drug utilization studies which also include evaluation of prescription patterns. Demand for drug utilization studies has increased with entry of newer costlier drugs in market and wide variation in the patterns of drugs being prescribed and consumed. Study of prescription patterns may be achieved by conducting prescription based surveys which give insight of prescribing attitude of physicians.Such studies help to monitor specific therapeutic categories, adherence to regulatory authorities and

assessment of clinical efficacy thus promoting rational use of drugs. The study of the prescription patterns of antihypertensive drugs and its correlation with blood pressure control helps in evaluating effectiveness of the management of HTN. It also focusses on commitment of the physicians to the recommendations of approved international guideline **[7].** In general, prescriptions are highly individualized and influenced by pharmaceutical marketing strategies, associated comorbid clinical conditions, tolerability of patient, adverse drug reactions, physician's knowledge and affordability of drug.

EXPERIMENTAL SECTION

The present study was conducted in a teaching hospital of Jaipur, (Rajasthan) to monitor rational use of antihypertensive drugs in hypertensive patients. This is a retrospective cross sectional analysis of anti-hypertensive prescriptions. Study included randomly selected prescriptions of hypertensive patients visiting various outpatient departments viz medicine, cardiology, endocrinology, neurology, nephrology over a period of three months (July, August and September, 2015) in a teaching hospital of Jaipur (Rajasthan). Patients with any stage of hypertension with or without co-morbidities were included in the study. Prescriptions of pregnant women, children below 18 years of age and the prescriptions on which diagnosis was not mentioned were not included in the study. Patient's demographics, antihypertensive drugs prescribed and comorbid conditions were entered in a specially designed proforma. Collected prescriptions were then segregated as per category of anti-hypertensive prescribed and data was pooled. Pooled data was then analyzed to draw inferences.

RESULTS

A total of 227prescriptions were monitored, of which 134 i.e. 59.03% were of males and 93 i.e. 40.96% were of females. It was observed that 29.9% prescriptions were of hypertension alone, 39.20% were of HTN with coronary artery disease (CAD), 18.50% were of hypertension with diabetes and remaining included patients of hypertension with associated comorbid diseases like chronic kidney disease, dyslipidemia, hypothyroidism, epilepsy etc. The age group of patients varied from 20-89 years. It was found that maximum number of hypertensive males were in 50-59 years of age group, whereas in females maximum cases of HTN were found to be in age group of 40-49 years (Table I).

Table I. Demographic characteristics of hypertensive patients undergoing monotherapy and combination therapy

Age groups (in years)	Male n= 134		Female n= 93		All patients n= 227	
20-29	4	(2.98%)	3	(3.22%)	7	(3.08%)
30-39	6	(4.47%)	11	(11.82%)	17	(7.48%)
40-49	33	(24.62%)	25	(26.88%)	58	(25.55%)
50-59	62	(46.26%)	40	(43.01%)	102	(44.93%)
60-69	21	(15.67%)	9	(9.67%)	30	(13.21%)
70-79	5	(3.73%)	3	(3.22%)	8	(3.52%)
80-89	3	(2.23%)	2	(2.15%)	5	(2.20%)
Monotherapy	39	(29.10%)	34	(36.55%)	73	(32.15%)
Combination	95	(70.89%)	59	(63.44%)	154	(67.84%)

Antihypertensive therapy was termed as monotherapy, dual therapy and multiple therapy, where single class of antihypertensive, two classes of antihypertensive and more than three classes of drugs respectively are used for the treatment.

Table II: Therapy prescribed in patients of Hypertension only

	MONOTHERAPY			DUAL THERAPY											TRIPLE THERAPY				
Drug	L	A	AT	L+ H	L+A	A+AT	L+AT	A+H	Li+M	L+To	L+M	Li+A	T+H	R+L	L+A+H	L+A+To	L+A+F	T+A+H	Li+A+F
n	16	6	3	14	7	7	2	2	1	1	1	1	1	1	1	1	1	1	1
%	64	24	12	36.84	18.42	18.42	5.26	5.26	2.63	2.63	2.63	2.63	2.63	2.63	20	20	20	20	20

L-Losartan, A- Amlodipine, AT- Atenolol, L+H- Losartan+Hydrochlorthiazide, L+A- Losartan+Amlodipine, A+AT- Amlodipine+Atenolol, L+AT- Losartan+Atenolol, A+H- Amlodipine+Hydrochlorthiazide, Li+M- Lisinopril+Metoprolol, L+To- Losartan+Torsemide, L+M- Losartan+Metoprolol, Li+A- Lisinopril+Amlodipine, T+H- Telmisartan+ Hydrochlorthiazide, R+L- Ramipril+Losartan, L+A+H- Losartan+ Amlodipine+ Hydrochlorthiazide, L+A+To- Losartan+Amlodipine+Torsemide, L+A+F- Losartan+Amlodipine+Frusemide, T+A+H- Telmisartan+Amlodipine+ Hydrochlorthiazide , Li+A+F- Lisinopril+ Amlodipine+Hydrochlorthiazide

The present study demonstrates that 68 patients were diagnosed with essential hypertension without any other comorbid disease out of which 25 patients were prescribed with monotherapy. The most preferred drug was found to

be losartan (64%) followed by amlodipine (24%) and atenolol (12%) respectively (Table II). In 38 patients dual therapy was prescribed (i.e. combination of two classes of antihypertensive). The most prescribed combination was losartan+hydrochlorthiazide (36.84%) followed by combination of losartan+amlodipine (18.42%) and amlodipine+atenolol (18.42%) (Table II). In only 5 prescriptions triple therapy was given. Switching over to three or more drug combinations is recommended in cases where dual therapy is unsuccessful in reaching the target blood pressure. **[8]**

Outcome of the study revealed that out of 227 prescriptions with or without associated comorbid disease, 73 patients i.e. (32.15%) were under monotherapy, 126 (55.50%) patients were under two drug combination therapies, 23 (10.13%) patients received three drug regimen and only (2.20%) patients were treated with combination of four anti-hypertensives (Table III). It was observed that monotherapy was more prescribed in females (36.55%) while combination therapy was popular among males (70.89%) against (63.44%) in females (Table III). As monotherapy angiotensin receptor blockers (ARB) were the most commonly (52.05%) prescribed antihypertensive followed by calcium channel blockers (12.32%) and β-blocker (12.32%) with equal frequency. Also it was seen that among ARB's losartan was the first choice of doctors and alone contributed 97.43% whereas telmisartan contribution was found to be 2.56% only.

Table III. Drug therapy in patients of hypertension

DRUG THERAPY	NUMBER OF PATIENTS (n=227)					
	MALE (n=134)		FEMALE (n=93)		TOTAL (n= 227)	
Monotherapy	39	29.10%	34	36.55%	73	32.15%
Two drug combination	77	57.46%	49	52.68%	126	55.50%
Three drug combination	15	11.19%	8	8.60%	23	10.13%
Four drug combination	3	2.23%	2	2.15%	5	2.20%

n: number of patients

It was observed that nine different two-drug combinations were prescribed (table IV), of which combination of β-blocker with angiotensin converting enzyme inhibitor (ACEI) was most prescribed (26.62%) followed by ARB with diuretic (14.93%), ARB with calcium channel blocker (CCB) 14.28% and ARB with β-blocker (12.33%) respectively. Of allthe combinations most frequently prescribed combination were ramipril+metoprolol (92.68%) (especially in patients of HTN alongwith CAD), losartan+amlodipine (83.36%), losartan+hydrochlorthiazide (73.91%), amlodipine+atenolol (72.72%) followed by losartan+metoprolol (63.15%).

Table IV. Antihypertensive drug combination therapy in descending order of their prescribing frequency among male and female patients

COMBINATION THERAPY TWO DRUG COMBINATION	MALE n= 134		FEMALE n= 93		TOTAL n= 227	
ACEI+ βB	37	38.94%	4	6.77%	41	26.62%
ARB+DIURETIC	6	6.31%	17	28.81%	23	14.93%
ARB+CCB	10	10.52%	12	20.33%	22	14.28%
ARB+βB	14	14.73%	5	8.47%	19	12.33%
CCB+ βB	5	5.26%	6	10.16%	11	7.14%
ACEI+CCB	2	2.10%	2	3.38%	4	2.59%
ACEI+DIURETIC	1	1.05%	2	3.38%	3	1.94%
CCB+DIURETIC	1	1.05%	1	1.69%	2	1.29%
ACEI+ARB	1	1.05%	0	0	1	0.64%
Total	77		49		126	
THREE DRUG COMBINATIONS						
ARB+CCB+DIURETIC	6	6.31%	3	5.08%	9	5.84%
ACEI+ βB+DIURETIC	4	4.21%	1	1.69%	5	3.24%
CCB+ βB+DIURETIC	2	2.10%	2	3.38%	4	2.59%
ARB+ βB +DIURETIC	1	1.05%	1	1.69%	2	1.29%
ACEI+CCB+DIURETIC	0	0	1	1.69%	1	0.64%
ACEI+CCB+ βB	1	1.05%	0	0	1	0.64%
ACEI+ARB+DIURETIC	1	1.05%	0	0	1	0.64%
Total	15		8		23	
FOUR DRUG COMBINATIONS						
ATB+αB +βB+ DIURETIC	0	0	1	1.69%	1	0.64%
ATB+CCB+αB+ DIURETIC	1	1.05%	0	0	1	0.64%
ATB+CCB+βB + DIURETIC	1	1.05%	0	0	1	0.64%
ACEI+CCB+βB + DIURETIC	1	1.05%	1	1.69%	2	1.29%
Total	3		2		5	

Key- ACEI: Angiotensin Converting Enzyme Inhibitor; ARB: Angiotensin Receptor Blocker, CCB: Calcium Channel Blocker; βB: Beta Blocker; αB: Alpha Blocker

Regarding patients who were on triple drug regimen it was observed that angiotensin receptor blocker with a calcium channel blocker and a diuretic was prescribed to majority (39.13%) of patients and in this category losartan+amlodipine+hydrochlorthiazide was the leading (55.55%) combination. Further it was observed that ACEIs clubbed with a beta blocker and a diuretic was second (21.73%) most prescribed three drug regimen followed by combination of CCB with beta blocker and diuretic.(Table IV)

Four drug combinations were prescribed least (2.20%) and that too in associated co-morbid states for effective blood pressure management, likewise combination of losartan+prazocin+metoprolol+frusemide in elderly patients with complaints of hypertension with benign prostrate hyperplasia and chronic kidney disease.

DISCUSSION

Prescription based surveys helpsin improving prescribing practice of the physicians and ultimately, the clinical standards. Therefore to promote rational use of drugs a continuous supervision and systematic audit of prescriptions is necessary. Antihypertensive drugs prescribing pattern study comprising of 227 prescriptions revealed that 29.95%patients were suffering from essential hypertension, 39.20% patients HTN associated with CAD of which 42.1% were males of 50-59years. The outcome of the study demonstrated that combination therapy (67.84%) outweighed monotherapy (32.15%). Monotherapy was more used in females (36.55%) while combination therapy was preferred in males (70.89%). As per recommendations of JNC V, VI and VII diuretics are considered to be first line treatment for HTN, but in our study not even a single patient was prescribed with diuretic as monotherapy. In combination therapy, diuretics were prescribed in a fixed dose combination with angiotensin receptor blocker (losartan). In dual therapy this was the most prescribed combination in patients of essential hypertension. The under utilization of low cost diuretics in monotherapy in present study was found to be not in accordance with JNC VII. Preference to combination therapy is also evidenced from Hansson et al Hypertension Optimal Treatment (HOT) study in which 70% of patients were given combination therapy, of which 90% patients achieved diastolic blood pressure of <90 mm Hg**[9]**. Studies like Controlled Onset Verapamil Investigation of Cardiovascular Endpoints (CONVINCE) and International Verapamil-Trandolapril Study (INVEST) also confirmed combination therapy to be more effective in management of HTN as compared to monotherapy**[10], [11].**It may be attributed to multiple pressor mechanisms contributing in raising blood pressure so multiple inhibitory mechanisms are likely to be more effective than a single one. Also, the individual drug in a combination therapy counteracts feedback mechanisms that act to limit the efficacy of the other antihypertensive drug. Likewise, combining an ARB, an ACE inhibitor, or a β blocker with a thiazide diuretic are examples of logical combinations. These drugs compensate reactive hyperreninemia induced by diuretics. Furthermore, with coadministration, doses are lower than those required when the components are used as single agents. A once-daily dose formulation of the combination facilitates dosing and improves compliance**[12].**

Out of total 227 almost 160 hypertensive cases were found to be associated with comorbidities like diabetes mellitus, coronary artery disease, chronic kidney disease, dyslipidemia, hypothyroidism etc. The physicians are required to select suitable antihypertensive treatment following multiple recommendations and guidelines for such patients. The goal of treating such patients is to lower blood pressure and relieve the comorbid disease. In the study it was observed that in patients of HTN with CAD, combination of ACEI with beta blocker i.e. ramipril+metoprolol was most prescribed (65.78%) in males of 40-59 age group. Clinical data supporting these results may relate to modification of the remodeling process by beta blocker and ACE-inhibitors seem to prevent progressive left ventricular dilatation thus the combination results in slowing of disease progression and preservation of contractile function **[13].**Also, cardioselective beta blockers like metoprolol are more preferred to minimize adverse effects especially β1 mediated bronchoconstriction. Prescription pattern analysis demonstrated losartan to be an integral part in monotherapy as well as multiple therapies viz. losartan+amlodipine, losartan+hydrochlorthiazide especially in patients of HTN with diabetes. Further it was found that losartan is the most utilized antihypertensive agent in the present study. This may be attributed to benefit of losartan in reducing renal outcomes in patients with type 2 diabetes and proteinuria as demonstrated by Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) study **[14]**. In another study losartan was judged to be better than atenolol in reducing primary composite end point of cardiovascular mortality, stroke and myocardial infarction by Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) conducted on 9193 patients aged 55-80 years suffering from essential hypertension and left ventricular hypertrophy **[15]**.Preference of ARBs over ACEIs was further confirmed, due to angioedema with the latter **[16].**

CONCLUSION

The present study concludes that in Jaipur (Rajasthan) 70.04% of hypertensive patients are found to be associated with comorbid disease like coronary artery disease, chronic kidney disease, diabetes mellitus, hypothyroidism, etc. Low cost first line drugs diuretics are underutilized which is not in accordance with JNC VII. The most prescribed and most utilized antihypertensive agent is Losartan, an angiotensin receptor blocker. 67.84% patients received dual therapy and triple therapy was prescribed to only few patients who were found to have complicated hypertension.

Acknowledgement
I hereby acknowledge Marudhar Hospital (khatipura, Jaipur) for granting me permission to collect prescriptions and conduct survey. I am highly obliged to Dr. Ramesh Gupta (MD, Physician), Dr. Kapil Agrawal (Quality Manager) and Dr. Abhishek Chauhan (Administrator) for their help and support to conduct the study.

REFERENCES

[1] National Cardiovascular Disease Database. Sticker No: SE / 04 / 233208. Supported by Ministry of Health & Family Welfare, Government of India and World Health Organization: 1-36
[2] A global brief on hypertension. Silent killer, global public health crisis. World Health Day **2013**, WHO; 1-39
[3] Anchala R, Kannuri N.K., Pant H, Khana H, Franco O.H., Angelantonioa E.D., Prabhakarand D. *Journal of Hypertension*,**2014**, 32(6), 1170–1177
[4] Mohd A.H., Mateti U.V., Konuru V, Parmar M.Y., Kunduru B.R. *Perspectives in Clinical Research*,**2012**, 3(4), 139-142
[5] Gupta R. *Journal of Human Hypertension*, **2004**, 18, 73–78.
[6] Shukla A.N., Madan T, Thakkar B.M., Parmar M.M and Shah K.H. *Advances in Epidemiology*,**2015,** 1-5
[7] Drabah E.L., Irshaid Y, Yasein N, Zmeili S. *Medicine Science*,**2013,** 2(1), 469-88
[8] James P.A., Oparil S, Carter B.L., Cushman W.C., Himmelfarb C.D., Handler J, Daniel T. Lackland D.T., LeFevre M.L., MacKenzie T.D., Ogedegbe O, Smith S.C., Svetkey L.P., Taler S.J., Townsend R.R., Wright J.T., Narva A.S., Ortiz E. *American Medical Association,***2013,** E1-E14
[9] Hansson L, Zanchetti A, Carruthers S.G, Dahlöf B, Elmfeldt D, Julius S, Ménard J, Rahn K.H, Wedel H, Westerling S for the HOT Study Group. *The Lancet*, **1998**, 351, 1755-1762
[10] Black H.R., Elliott W.J., Neaton J.D., Grandits G, Grambsch P, Richard H. Grimm, Jr, Lennart Hansson, Yves Lacoucie`re, James Muller, Peter Sleight, Michael A. Weber, William B. White, Gordon Williams, Janet Wittes, Alberto Zanchetti, T. Daniel Fakouhi, Robert J. Anders.*Hypertension*,**2001,** 37, 12-18.
[11] Pepine CJ, Handberg EM, Cooper-DeHoff RM, Marks RG, Kowey P, Messerli FH, Mancia G, Cangiano JL, Garcia-Barreto D, Keltai M, Erdine S, Bristol HA, Kolb HR, Bakris GL, Cohen JD, Parmley WW. *JAMA*,**2003,** 290(21), 2805-16
[12] Kalra S, Kalra B, Agrawal N. *Diabetology & Metabolic Syndrome*, **2010,** 2(44), 2-11
[13] Khattar RS. *Minerva Cardioangiologica*,**2003,** 51(2),143-54
[14] Shahinfar S.S, Dickson T.Z., Ahmed T, Zhang Z, Ramjit D, Smith R.D. and Brenner B.M. *Kidney International*,**2002,** 62, Supplement 82:S64–S67
[15] Dahlöf B, Devereux RB, Kjeldsen SE, Julius S, Beevers G, de Faire U, Fyhrquist F, Ibsen H, Kristiansson K, Lederballe-Pedersen O, Lindholm LH, Nieminen MS, Omvik P, Oparil S, Wedel H.*Lancet*,**2002,** 359(9311), 995-1003
[16] Palatini P. *The Journal of Clinical Hypertension*,**2005,** 7, 96-101