



Drug Utilization Study of Antihypertensive Medication in Both Sex and Different Age Group attending at Medicine Outpatient Department of a Tertiary Care Hospital

Abhijit Das¹, Sahin Parvin², Avijit Ganguly^{3*}, Saswati Sarkar⁴, Milan Chakraborty⁵

^{1 & 3*} Department of Pharmacology, R. G. Kar Medical College, Kolkata, INDIA

² Bengal School of Technology, Hooghly, West Bengal, INDIA

⁴ Department of pharmacology, Burdwan Medical College, Burdwan, West Bengal, INDIA

⁵ Department of Medicine, R. G. Kar Medical College, Kolkata, INDIA

* Correspondance: E-mail: avijitdec81@gmail.com

(Received 02 April, 2015; Accepted 02 May, 2015; Published 28 May, 2015)

ABSTRACT: To observe prescription pattern of different drugs in different age & sex groups with or without comorbidities with the aim of formulating local guidelines in the management of Hypertension in future. Over the period of nine months hypertensive subjects of all age groups were observed attending Medicine Outpatient Department (OPD) of R. G. Kar Medical College & Hospital, Kolkata. Many of whom have comorbidities like coronary artery disease, heart failure, diabetes, dyslipidaemia, bronchial asthma, COPD etc. Pregnant and hypertension due to secondary causes were excluded. Name of the prescribed antihypertensive drug(s), their dose and duration of treatment were noted. Among 250 subjects 115(46%) were male & 135(54%) female. Among all subjects 80(32%) were less than 40yr group, 129 patients (51.6%) are middle aged (40-60 yrs.). Seventy two percent (180) patients were on monotherapy and rest on multiple drugs. Amlodipine was found to be the most preferred agent of monotherapy (43 or 17.2%). One hundred and twenty three patients were with some co-morbidities. As per BHS/NICE guideline, 2011 ACEI/ARB's should be used much more than any other anti-hypertensive, but here Amlodipine was used much more. The scope of multi drug therapy is actually higher as per the guideline but, here the use of multi-drug therapy is less than that recommended.

Keywords: Drug utilization; Antihypertensive drugs; Telmisartan; Amlodipine; Enalapril, Hydrochlorothiazide; Standard guidelines.

INTRODUCTION: Hypertension can be defined as any one of the following criteria: Systolic blood pressure ≥ 140 mmhg or diastolic blood pressure ≥ 90 mmhg or patient taking antihypertensive medication¹. It is a commonest cardiovascular disorder, posing a major public health challenge to population in socio-economic and epidemiological transition². In vast majority (>98%) of patients with essential hypertension, it is likely that hypertension represent a polygenic disorder in which a combination of genes acts in concert with environmental exposure. Further, different subsets of genes may lead to different phenotypes associated with hypertension. e.g.: obesity, dyslipidaemia, Insulin resistance etc. Current evidence suggests that genes that encode components of the renin-angiotensin-aldosterone system, along with angiotensinogen and angiotensin-converting enzyme (ACE) polymorphisms related to hypertension. The alpha-adducingene, genes that encoding angiotensin 1 receptor (AT1), aldosterone synthase and β 2adrenoreceptor are also related with hypertension³.

According to JNC 7, Hypertension can be treated with

single (monotherapy) or multiple drugs (combination therapy) to reach the target B.P⁴.

Data from a very large multicentre RCT⁵ supported by smaller studies demonstrate that moderate-to-high dose thiazide diuretics (chlorthalidone 25 mg/day or its equivalent of HCTZ, about 50mg/day) are as good as any other class of agents in reducing cardiovascular adverse outcomes, and superior in secondary outcomes such as stroke and CHF. Most patients will require two or more drugs to achieve control, and a few will not tolerate thiazides. The choice of additional or alternative medication should be individualized to achieve the target BP and the following goals⁶:

- Once daily administration
- Reduction in CV complications demonstrated in clinical trials
- Choice of agent(s) that also treat concurrent conditions
- Least potential disruptive side-effects based on concurrent conditions or lifestyles
- Least expensive (both in pharmaceutical and laboratory monitoring costs)

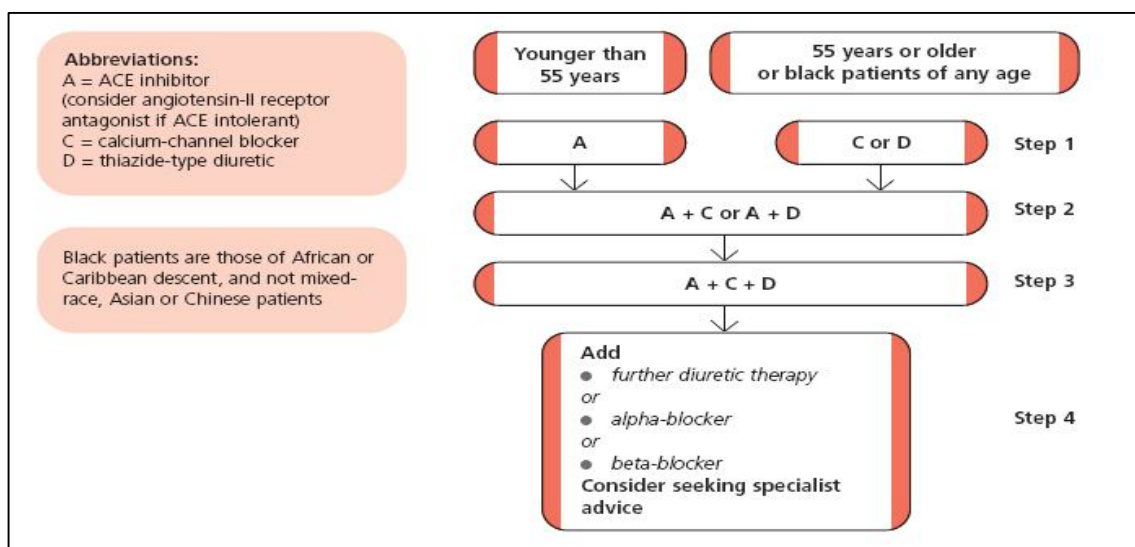


Figure 1: Choosing drugs for patients newly diagnosed with hypertension.

Fixed combination therapy can be more cost effective and may improve compliance. Some patients may benefit from beginning with fixed combination therapy (e.g., Stage 2 hypertension or patients resistant to monotherapy in the past).

If monotherapy is not effective in reaching the BP goal, the addition or substitution of a different class with different physiological action is indicated. Combining medications from the same class is not effective⁷. Diuretics, beta blockers, ACE inhibitors, and long-acting dihydropyridine CCBs have been shown in randomized controlled trials to reduce cardiovascular morbidity and mortality. The ALLHAT study was a large multicenter direct comparison RCT⁵ designed to determine if the older or newer agents are more effective in prevention of cardiovascular morbidity and mortality. It compared treatment starting with a thiazide diuretic, an ACE inhibitor, a long-acting dihydropyridine CCB and an alpha-blocker. Beta blockers and centrally-acting agents were used as the second step drugs. Almost three-fourths of patients required two or more drugs. Beta blockers were the most commonly used second agent. The alpha blocker arm was discontinued early because of an excess of adverse effects. Angiotensin converting enzyme (ACE) inhibitors, as a class, have similar actions and side effects, with the only major difference being duration of action. ACE inhibitors reduce BP with generally few side effects and slow the decline of renal function in most diseases. Ramipril was shown in randomized controlled trial to decrease cardiovascular events in hypertensive and normotensive individuals with systolic heart failure over placebo⁸. However, newer trials have not shown renin-angiotensin blockade to be superior to other medications in decreasing morbidity and mortality. Onset of diabetes was not prevented by ramipril in a study directly addressing

this issue⁹.

For the management of hypertension, there is a guideline issued by British Hypertensive Society (BHS) and National Institute for health and Clinical Excellence (NICE), 2011 states that¹⁰, antihypertensive drug selection¹² as Figure 1.

MATERIAL AND METHODS:

1. Study design, aims and objectives:

1.1 Selection criteria: Study subjects were newly diagnosed hypertensive patients (Blood pressure >140/90mmHg) of both sexes and all ages attending the medicine outpatient department (OPD) over the study period of six months in between September 2013 to February 2014. After initial screening they were subdivided into groups according to sex, age (younger age group <40yrs, middle age group 40 to 60yrs, elderly age group >60yrs), & with or without co-morbidities. We excluded patients with hypertension of secondary cause or severely ill requiring hospitalization, pregnant & immunocompromized.

The study was approved by the Ethics Committee of R. G. Kar Medical College and Hospital, Kolkata, in August 2013. Diagnosis was done by attending physicians at Medicine OPD of R. G. Kar Medical College.

1.2 Aims and Objectives:

I. To observe prescription pattern of different drugs in different age & sex group with or without co-morbidities.

II. Aim of formulating local guidelines in the management of Hypertension in future.

2. Activities at time of visits: The screening assessment after diagnosis was confirmed, the selection criteria were checked. Written informed consent was sought. A general examination including weight,

length/height of the subject was undertaken. All anti-hypertensive medications prescribed are noted along with medications of other comorbidities. All subjects there after advised follow up monthly for next three months. During each visit apart from medication check; weight, B.P. and other parameters were noted.

RESULTS AND DISCUSSION:

Among 250 subjects 115(46%) were male & 135(54%) female. Among all subjects 80(32%) were less than 40yr group, 129 patients (51.6%) are middle aged (40-60 yrs.)(Table 1). Forty one patients (16.4%) are elder patients.

Seventy two percent (180) patients were on monotherapy and rest on multiple drugs. Some of the patients (Fig. 1) (46 or 18.8%) were on fixed dose combinations of antihypertensives. Amlodipine was found to be the most preferred agent of monotherapy (43 or 17.2%), followed by Enalapril (22 or 8.8%) and Olmesartan (11 or 4.4%). Among those receiving multiple medicines (Figure 2 & 3); Amlodipine and Enalapril as separate tablets (Figure 4 & 5) (21 or 8.4%) and FDC of Telmisartan plus hydrochlorthiazide were prescribed mostly (20 or 8%)(Table 2). One hundred and twenty three patients were with some co-morbidities along with hypertension.

Table 1: Demographic distribution of Antihypertensive patients.

Age group	Male	Female	Total	Percentage
<40 yrs	39	41	80	32%
40-60yrs	55	74	129	51.6%
>60yrs	21	20	41	16.4%
Total	115 (46%)	135 (54%)	250	100%

Table 2: Sex distribution pattern of Monotherapy Versus Multidrug therapy.

	Male	Female	Total
Monotherapy	80	100	180(72%)
Multidrug therapy	34	36	70(28%)

As per guideline^{10 & 11}, in monotherapy drugs like ACE inhibitors/ARB's should be prescribed first as younger as well as middle age group but in our study in this institution instead of ACEI/ARB's, amlodipine is used much more(75%) totally.

In case of multidrug therapy, Patients who could not reach the target BP with monotherapy or the patients with stage II hypertension should be treated with multidrug therapy. Here, the use of multidrug therapy is much lower than it should being our study in this institution. This is right according to our results. Because in our study we shown that the most of the pa-

tients who received monotherapy reaches the target goal and the stage I hypertensive patients are more than stage II hypertensive patients. In our study it was clearly shown that the incidents of diabetes with hypertensive is quite common, the percentage is 25.6.

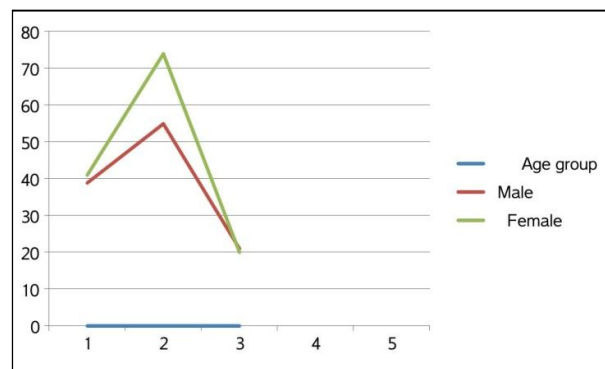


Figure 2: Frequency of free drug combinations and fixed drug combination.

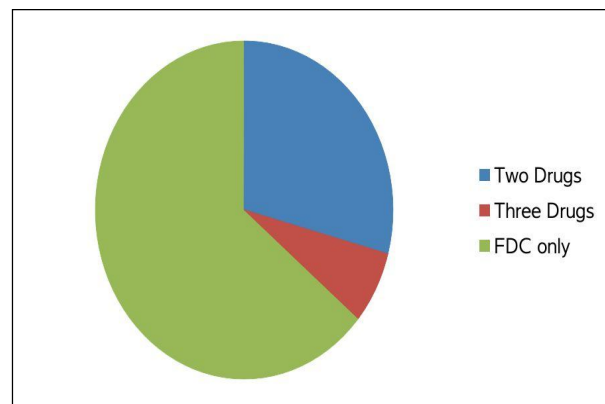


Figure 3: Frequency of fixed drug combinations in pie chart.

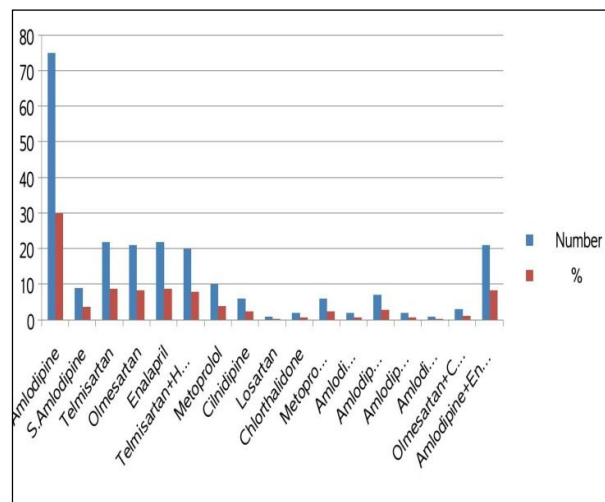


Figure 4: Percentage distribution of different combination of drugs.

According to ADA treatment guideline 2015¹¹, all the hypertensive patients with diabetes should be treated

with ACEI/ARB unless otherwise contraindicated. In our study here we also see that the use of ACE inhibitors or ARB's is much less than it should be: In case of monotherapy 5mg dose of Amlodipine is used much more, in case of S. Amlodipine the dose is also 5mg. In case of Telmisartan this is 40mg, in Olmesartan that is 40mg also. In case of Enalapril that is 5mg. In Losartan 25mg dose is used more. In chlorthalidone, Metoprolol and Cilnidipine the dose is 6.25mg, 25mg and 10mg respectively is more used.

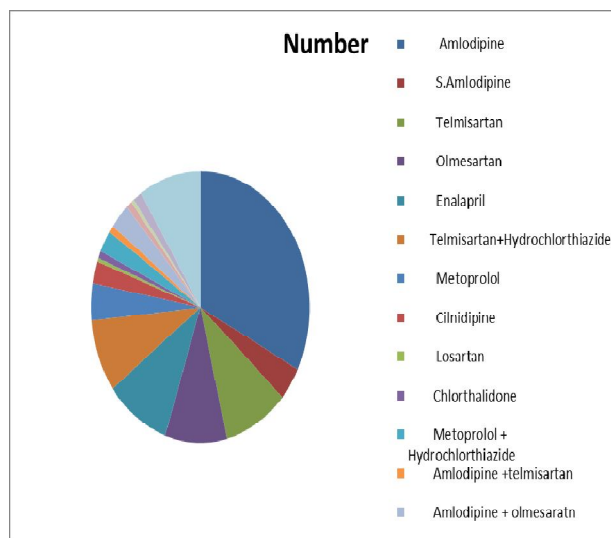


Figure 5: Drug distribution pattern pie chart.

Generic names have been used in over 50% encounters of antihypertensive drug. Three key antihypertensive drugs (amlodipine, telmisartan, enalapril) were being supplied by hospital pharmacy. About 50% drugs were prescribed from essential drug list which included

Some adverse drug events were noted during the study period that were reported to the ADR monitoring centred R.G. Kar medical College, department of pharmacology.

We found that DU 90% in this study comprised of amlodipine, telmisartan, enalapril. As per BHS/NICE guideline, 2011¹⁰ & ¹² ACEI/ARB's should be used much more than any other anti hypertensive. But, here Amlodipine is used much more. The scope of multi drug therapy is actually higher as per the guide line. But, here the use of multidrug therapy is less than that recommended.

Problems and Interceptive Measures Suggested: The most important problem identified during this study is poor compliance to antihypertensive Drug. Overall compliance was only 40%. Knowledge regarding proper dosage of drugs was found only in 60% encounters.

Most of the patients in this study did receive oral anti-hypertensive drugs from hospital pharmacy. But the

drugs were being supplied for a fortnight period. In most of the cases the patients failed to come every fortnight for receiving antihypertensive drugs and discontinued the drugs resulting in poor control of blood pressure status. This got reflected in the fact that only in 40% encounters target blood pressure was reached.

This problem can be addressed to some extent by supplying oral antihypertensive drugs for at least one month to patient in each visit. Besides the patients need to be educated regarding the important of proper blood pressure controlled to prevent microvascular and macrovascular complication. This patient education can be done by treating physician or separate persons like patient care educators.

But the average consultation time between patient and treating physician has been only 3.5 minutes (probably because of huge patient load in the Medicine OPD of this hospital) which is not sufficient for proper patient education. So either average consultation time has to be increased or the authority should recruit patient care educators separately. This will enhance the compliance and knowledge of the patients regarding proper drugs dosage which will help to achieve the target blood pressure goal.

The second most problem encountered in the study was lack of knowledge regarding proper medical nutrition therapy and non-compliance to regular aerobic exercise. Only 40 out of 250 patients had proper idea about medical nutrition therapy and 90 out of 250 patients were complained regular aerobic exercises. This aerobic exercise with medical nutrition therapy forms the back bone of life style modification treatment in hypertension.

We were unable to provide diet chart to the patients due to lack of resources. Most of the time they were given dietary advises only during their first time visits which were not put into practice every time. So the need for a dietician is essential¹² in blood pressure clinic who can prepare a diet chart according to the need of individual hypertensive.

Thirdly, diabetes has not been properly control in most of the hypertensive patients. Though most of the antidiabetic agents are available in hospital pharmacy treating physician should be more enthusiastic in controlling diabetics.

CONCLUSION:

We found that most of the patients belonged to middle age group but ideally elderly age group patient population would be more. The female and male ratio was almost equal which is as per as other studies.

Among the co morbidities diabetes mellitus is the most common which is also at par with other studies. The ideal antihypertensive agent in diabetic patient is

either ACE/ARB¹³. But in our study in this institution Amlodipine was used more than that.

A large study is actually required to evaluate all this data properly.

Conflict of interest: No author has any conflict of interest to any company or professional body.

REFERENCES:

1. August P. (2003) Initial treatment of hypertension, *N. Engl. J. Med.*, 348, 610. Park's Textbook of preventive and social Medicine (20th edition)
2. WHO (1996) *Techn. Rep. Ser.*, 862.
3. Lawes C. M. M. et. al. (2008) Global burden of blood pressure-related disease, *Lancet* 371, 1513.
4. Chobanian A. V. et. al. (2003) The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, The JNC 7 Report, *JAMA*, 289, 2560.
5. ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group (2002) Major outcomes of high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blockers vs diuretic: The antihypertensive and lipid-lowering treatment to prevent heart attack trial, *JAMA*, 288, 2981.
6. Chalmer J. (1999) Importants of drug combination for effective control of hypertension, *Clin Exp hypertense*, 875-84.
7. Casas J. P. et. al. (2005) Effect of inhibitors of the renin-angiotensin system and other antihypertensive drugs on renal outcomes: Systematic review and meta-analysis, *Lancet*, 366, 2026.
8. The Heart outcome prevention Evaluation study investigation (2000) Effect of as angiotensin-converting enzyme inhibitor, ramipril on cardio vascular events in high risk patients. *N. England Journal of medicine*, 342,145-153.
9. National Institute for Health & Clinical Excellence. Clinical management of primary hypertension in adult, (2011).
10. British Hypertensive Society Guideline (2006) algorithm for choosing drug for the patients newly diagnosed with hypertension.
11. American Diabetes Association (2011) Standards of medical care in diabetes. *Diabetes Care* 34:S11.
12. Vollmer W. M. et. al. (2001) Effects of diet and sodium intake on blood pressure: Subgroup analysis of the DASH-Sodium trial, *Ann Intern Med.*, 135, 1019.
13. Kaplan N. M. (2001) Management of hypertension in patients with type 2 diabetes mellitus: Guidelines based on current evidence, *Ann Intern Med.*, 135, 1079.