ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES Knowledge to Innovation

Vol 6, Suppl 3, 2013

ISSN - 0974-2441

Research Article

COMPARATIVE STUDY OF FIXED DOSE COMBINATION OF OLMESARTAN+AMLODIPINE VS TELMESARTAN+METOPROLOL IN STAGE I AND STAGE II HYPERTENSIVE PATIENTS AND ALSO CHECK THEIR EFFECTS ON LIPID METABOLISM.

VIRAG SHEKHAR SHAH*[1], PITAMBAR NILKANTH DIGHORE[2], HETAL ATULBHAI PATEL[3], SUGHOSH VISHWESHWER UPASANI[4]

[1] Management Trainee, Clinical Research department, Micro Advance Research Center, Bangalore 560068, [2]General Physician at Indira Gandhi Memorial Hospital Shirpur-425405, M.S. India, [3] Department of Clinical Pharmacy, R.C.Patel Institute of Pharmaceutical Education and Research, Shirpur-425405 M.S India, [4] Assistant Professor, department of Pharmacology and Clinical Pharmacy. Smt. S.S.Patil College of Pharmacy, Chopda- 425107, Dist- Jalgaon M.S, India. E-mail: viragshah27@gmail.com

Received: 23 May 2013 Revised and Accepted:19 June 2013

ABSTRACT

Objectives - Hypertension is the second most severe problem after diabetes in India for the mortality rate. So the primary goal to reduce the mortality is to achieving targeted blood pressure in an individual. Hypertension guidelines recommend the use of 2 agents having complementary mechanisms of action when >1 agent is needed to achieve blood pressure (BP) goals. The objectives of this study are to compare the effect of combination on BP, Lipid Profile, and also to check the safety of both combinations. Methods- This is 16 week open label, study, in which total 70 patient were enrolled. The study was carried out at outpatient department of Indira Gandhi Memorial Hospital Shirpur, Dist- dhule. We include patients which are newly diagnosed to hypertension. Permission from Institutional Human Ethical Committee was obtained. Results- combination therapies shows greater effects on lowering blood pressure than individual monotherapies. In our study we found group II combination shows greater effect than group I combination. The mean BP reduction was found to be ± 31.9/ 13.05 in group I, while in group II ±33.24/15.59 mmHg in group II from baseline after three months follow-up for systolic and diastolic respectively. While comparing lipid profile again Group II shows better results than Group I. Conclusion- These finding shows that the group II shows greater efficacy than group I in all parameter evaluated. The finding also shows that both the combinations are safe and efficacious.

Keywords: Hypertension, Olmesartan, Amlodipine, Telmesartan, Metoprolol, combination therapy, Lipid Profile, Fixed Dose Combination.

INTRODUCTION

Hypertension is a common disease that is simply defined as persistently elevated arterial blood pressure (BP) which is a biological variable and so absolute values could be different based on the clinical circumstance e.g. pediatrics, pregnancy and isolated systolic hypertension. Thus the only numerical variable in this classification is the normal BP value. [1] Increasing awareness and diagnosis of hypertension, and improving control of BP with appropriate treatment, are considered critical public health initiatives to reduce Cardio Vascular (CV) morbidity and mortality.

The Seventh Report of the Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure (JNC VII) is the most prominent evidence-based clinical guideline in the United States for the management of hypertension, supplemented by the 2007. [2,3] Hypertension is a common cardiovascular problem worldwide. As with any other disease it is important to assess its severity. However the present classification of hypertension by the Joint National Committee in its seventh report with numerical values staging the severity of hypertension is theoretically correct but difficult to apply in practice.

Table 1: Classification of Hypertension [4, 5]

Category	Systolic BP (mmHg)	Diastolic BP (mmHg)
Normal	< 120	< 80
Pre Hypertension	120-139	80-89
Stage 1	140-159	90-99
Stage 2	≥ 160-179	≥ 100-109

Table 2: Antihypertensive combinations available in market. [4]

Combination Type	Fixed-Dose Combination, mg
ACEIs and CCBs	Amlodipine-benazepril HCL (2.5/10, 5/10, 5/20) Enalapril-felodipine (5/5)
ACEIs and diuretics	Benazepril-hydrochlorothiazide (5/6.25, 10/12.5, 20/12.5) Captopril-hydrochlorothiazide (25/15, 25/25, 50/15, 50/25)
ARBs and diuretics	Losartan-hydrochlorothiazide (50/12.5, 100/25) Olmesartan l-hydrochlorothiazide (20/12.5,40/12.5,40/25)
β-blockers and diuretics	Atenolol-chlorthalidone (50/25, 100/25) Bisoprolol-hydrochlorothiazide (2.5/6.25, 5/6.25, 10/6.25)
Centrally acting drug and diuretics	Methyldopa-hydrochlorothiazide (250/15, 500/30, 500/50) Reserpine-chlothalidone (0.125/25, 0.25/50)
Diuretic and diuretic	Amiloride-hydrochlorothiazide (5/50) Spironolactone-hydrochlorothiazide (25/25, 50/50)
ARB + CCB	Olmesartan + Amlodipine (20/2.5, 40/5, 80/10)

β-blockers + ARB	Telmesartan + Metoprolol (20/2.5, 40/5, 80/10)

MATERIALS AND METHODS

This study involves Comparative study of fixed dose combination of antihypertensive drugs Olmesartan +Amlodipine vs. Telmesartan + Metoprolol in stage I and stage II hypertensive patients and also to check the Lipid metabolism. Institutional Human Ethical committee letter were taken to perform human study.

Study Site

The study was conducted at outpatient department of Indira Gandhi Memorial Hospital Shirpur, Dhule district. The protocol was approved by Institutional Human ethical committee of R.C.Patel Institute of Pharmaceutical Education and Research, Shirpur.

Study Design and Duration

The controlled and observational study to evaluate safety and efficacy of antihypertensive combination in management of stage-1 and stage-2 hypertensive patients for 8-10 Months (From July to April)

Source of Data

The OPD Cards, Treatment Charts, Patient History, Laboratory Reports, Verbal communication with patients and patient data entry format called "Proforma" was prepared in order to collect all the essential information.

Selection of patients

Inclusion Criteria

Age between 30-70 years, Gender:- Both (Male/Female), Patient having mild to moderate hypertension Stage-1 SBP- 140-159mmHg DBP-90-99mmHg Stage-2 SBP ≥ 160mmHg (Mild Hypertension) DBP ≥ 100mmHg (moderate hypertension) **Exclusion Criteria**

Secondary or malignant hypertension, patient having renal failure, pregnant and lactating women, history of serious adverse reaction to angiotensin II receptor blockers or calcium channel blockers.

Distribution of patients

The patients were distributed into two groups as follows

Group I- Telmesartan + Metoprolol

Group II- Olmesartan + Amlodipine

RESULTS

Patient Variables

The different patient's characteristic like age, sex BMI, habit, diet, etc is shown in following table.

Blood Pressure

Significant change was observed in group II as compare to group I. The percentage change in BP for both groups is shown in following tables.

Table 3: Patient's variables

Variables	Group I	Group II
Number of Patients	N=36	N=34
Age(Yrs)	52.70 ± 10.89	53.80± 14.46
Sex Male / Female	13 / 23	18 / 16
BMI	20.02 ± 4.08	19.07 ± 4.14
Smoker / Non-Smoker	7 / 29	12 / 22
Alcoholic / Nonalcoholic	3 / 33	7 / 27
Vegetarian / Mixed Diet	16 / 30	14 / 10

Table 4: Change in BP for Group I

Blood Pressure	Type	Mean Level	%change	P value
Baseline	Systolic	163.05 ± 13.09	-	
	Diastolic	93.05 ± 8.80	-	<0.0001****
1st Follow up	Systolic	150.88 ± 13.65	7.46%	Normal Value
	Diastolic	85.55 ± 6.06	8.06%	(P < 0.05)
2nd Follow up	Systolic	138.61 ± 11.25	8.13%	
	Diastolic	82.77 ± 7.01	3.42%	
3rd Follow up	Systolic	131.11 ± 7.47	5.41%	
	Diastolic	80.00 ± 4.78	3.26%	
Total Change from Baseline	Systolic	--	21.02%	
	Diastolic	--	14.74%	

Table 5: Change in BP for Group II

Blood Pressure		Mean Level	%change	P value
Baseline	Systolic	159.41 ± 16.68	-	<0.0001****
	Diastolic	93.82 ± 9.2	-	Normal Value
1st Follow up	Systolic	144.1 ± 13.51	9.59%	(P < 0.05)
	Diastolic	83.88 ± 6.03	10.57%	
2nd Follow up	Systolic	134.70 ± 13.53	6.52%	
	Diastolic	82.94 ± 6.75	1.02%	
3rd Follow up	Systolic	126.17 ± 8.17	6.33%	
	Diastolic	78.23 ± 6.72	5.63%	
Total Change from Baseline	Systolic		22.44%	
	Diastolic		17.15%	

Lipid Profile

Lipid profile was carried out for all patients at baseline and at end only for those who completed the study. Lipid profile contains cholesterol, triglycerides, high density lipoprotein, low density lipoprotein.

Table 6: Change in Lipid Profile for Group I

	TC (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL(mg/dl)
Baseline	188.84±45.11	153.03±46.78	57.62±17.61	98.49±45.79

End Study	177.66±38.04	141.97±38.61	53.94±17.93	89.97±37.23
% Change	5.92%	7.27%	6.38%	8.65%
p value	0.0385*	0.0482*	0.0360*	0.5224 NS

Table 7: Change in Lipid Profile for Group II

	TC (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)
Baseline	197.34±54.62	148.35±33.64	58.78±15.92	108.98±29.25
End Study	181.39±39.59	138.19±28.88	53.57±14.57	83.61±28.32
% Change	8.08%	6.84%	8.86%	23.27%
p value	0.0247*	0.0095**	0.0423*	0.0083**

DISCUSSION

In this study more than 86 patients visited to the outpatient department of medicine ward of Indira Gandhi Memorial Hospital Shirpur, amongst 86 patients 70 patients were completed the study with regular follow ups. Demographic parameters were done considering age, sex and body mass index. In Ibrahim A. Bani study it was shown that the male patients are more vulnerable for hypertension than female, again in Ibrahim A. Bani study they also shown that after some years of hypertension chances of developing myocardial infarction is greater in male than in female. But in our study we found some controversial results like more number of female than male. As the duration of study is limited we didn't get result regarding myocardial infarction. [8] Concerning with age factor Carmel M McEniery study shows that the middle age group that is after 40 years the chances of hypertension are increases and if patients is already suffering from hypertension after 40 years the chances of cardiac complication is increases, ageing is strongly associated with the development of isolated systolic hypertension, probably the most common clinical manifestation of arterial stiffening and a condition associated with considerable excess cardiovascular risk. [9] In this study we too found the more number of patients including both sex between age group of 31-50 years, additional research study stated that the complication of hypertension is increases with age [10] but in current study we found more number of patients between 31-50 years then 52-65 years, and 66-80 years. The main reason for increasing hypertension with age is the stiffness in arteries and due to this the resistance to blood flow is increases which lead to rise in blood pressure. There are some other factors that deposition of cholesterol in arteries and blockade of arteries and veins.

Along with age and sex, BMI also affect largely on cardiovascular risk mostly on hypertension. Previous study shows that if patients remain in category of same body mass index there will be slightly decrease in blood pressure, but if the patients BMI increases there may also increase the chance of cardiovascular risk. The conclusion of previous study stated that the results showed a higher trend of hypertension with increasing BMI. In young females it was noted that with a shift from normal BMI the incidence of hypertension was very high. In our study we found that more number of patients from normal BMI category these all patients are newly diagnosed hypertensive patients. During the study period we got only two obese patients after this more number of patients was from the underweight category, number of overweight patients was also less. This result is to some extent notorious with previous studies. Jay S Kaufman study shows that blood pressure increases with increasing body mass index, and overweight and/or obese patients are at high risk of hypertension [11] but in present study we found more patients in normal category than in overweight and/or obese patients. Now moving towards efficacy parameters firstly pulse rate and then blood pressure. J. C. VAILE study shows that there is no significant change in pulse rate and / or heart rate during the antihypertensive treatment such as calcium channel blockers and angiotensin receptor blockers. [12] In our study group I contain the combination of same category; our result is not momentous with VAILE study because in group I pulse rate decreased up to 19%. Sripal Bangalore study shows that those β- blockers like Metoprolol cause reduction in pulse rate in myocardial infarction and little decrease in normal hypertensive patients with no cardiac complications. [13] Present study result is significant with Sripal Bangalore study; because our study shows that great decrease in pulse rate in group II which contain β- blockers and angiotensin receptor blockers combination. In this group 24% decrease in heart rate / pulse rate. While considering result all the treatment group shows the significant decrease in value from baseline for the blood pressure. In Steven G. Chrysant study, result shows that the combination of Olmesartan Amlodipine shows greater reduction in systolic as well as diastolic blood pressure the finding of this study shows 19.2% reduction in systolic blood pressure from baseline and 23.0% reduction in diastolic blood pressure from baseline. [14] During our study we also got the significant reduction in systolic as well as diastolic blood pressure, we found 21.02% change in systolic blood pressure from baseline and 14.74% decrease in diastolic blood pressure from baseline. In present study we got fairly significant result with earlier studies cholesterol level decreases 6% from baseline, then triglycerides, high density lipoprotein, low density lipoprotein the value of these parameters is also decreased by 7.2%, 6.3%, and 8.6% respectively from baseline and for the group I which contain angiotensin receptor blockers and calcium channel blockers. Another group is group II which contains angiotensin receptor blockers and β-blockers. This group shows the result as follows 8.08%, 6.8%, 8.86% and 23.6% for cholesterol, triglycerides, high density lipoprotein, and low density lipoprotein correspondingly; this study shows significant result with previous studies. [15, 16]

CONCLUSION

Comparative study of antihypertensive drug combinations Olmesartan + Amlodipine Vs Telmesartan + Metoprolol in hypertensive patients was successfully carried out at outpatient department of Indira Gandhi Memorial Hospital Shirpur during the study period August to March. According to this comparative randomize study we can conclude that both the combination shows good blood pressure lowering effects, as well as lipid lowering effect and ultimately reduces the risk of onset of cardiovascular diseases among this combinations the group two combination which contain Olmesartan + Amlodipine follows under category of angiotensin receptor blockers + Calcium channel blockers shows better effect than group I combination which contains Telmesartan + Metoprolol follows under category of angiotensin receptor blockers + β-blockers. During the entire study period none of the patients complaints any side effects or adverse effects of both combinations, so from this we can conclude that both the combinations are safe, well tolerated, and effective in lowering blood pressure in type I and type II hypertensive patients

ACKNOWLEDGEMENT

I heartily thankful to all my colleagues for their valuable guidance and suggestion, I acknowledges to the Indira Gandhi Memorial Hospital, Shirpur's staff and the patients who are actively participated in this study. I would also like to extend my thanks to the Dr. S.J. Surana, **(Principal),** Dr. P.H.Patil, **(HOD)** Asst. Prof. V.G.Kuchake, and Asso. Prof. P.V.Ingle, Dept. of Clinical Pharmacy. R. C. Patel Institute of Pharmaceutical Education and Research, Shirpur, for the facilities

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