http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v8i7.81

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

To study the effect of Olmesartan medoxamil in patients with hypertension

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Abstract

Introduction: *Hypertension (high blood pressure) affects approximately 1 billion individuals worldwide. Epidemiological studies show a steadily increasing trend in hypertension prevalence over the last 40 years, more in urban than in the rural areas. Newer antihypertensive agents are constantly being introduced and heavily promoted. At present several Angiotensin receptor blockers (ARBs) are in use for the treatment of hypertension, heart failure and diabetic nephropathy. The newest agent in the class is Olmesartan medoxomil approved by FDA in April 2002 and widely used since then. By this study we will analyze the clinical outcome of Olmesartan medoxamil in patient with hypertension.*

Objectives: *To study the changes in BP, ECG and ECHO finding from baseline after giving Olmesartan.*

Material & Methods: *The present prospective study was carried out on 39 cases with 18-70 years age group diagnosed as hypertension (stage I and stage II - JNC7). After taking written informed consent detail history, demographic and clinical data, past medical and family history; presenting symptoms and signs; physical examination findings, BP, Hematological and Biochemical parameters ECG and ECHO findings were recorded in preformed proformas. Olmesartan 20 mg/day was given as starting dose and further increased if BP not controlled. All cases will be registered and followed up after at 3 month and 6-month. Blood pressure, ECG and, left ventricle (LV) dimensions and Left ventricular mass index (LVMI) by Echocardiography will be measured and data will be compared by appropriate statistical tests.*

Result: *In our study mean reduction in SBP and DBP from baseline to after three months of treatment was 6.72±7.54($P < 0.0001$) and 6.94±6.16 ($P < 0.0001$) and after 6 months was 10.16±9.57 ($P < 0.001$) and 9.38±6.56 ($P < 0.001$).On comparison between mean LVMI at baseline (43.23%) and after 3 months (42.65%) mean reduction was 0.57±1.01($P=0.12$, not significant) after 6 month (41.30%) the mean reduction was 1.93±2.10 ($P=0.025$, significant).*

Conclusion: *Olmesartan medoxomil at the recommended dose of 20 mg once daily will be effective in treatment of essential hypertension but was not effective in regression of ECG based left ventricular hypertrophy. Olmesartan medoxomil after treatment reduced the left ventricular mass index which was statistically significant. This study will be served as a pilot study for future research.*

Keywords: *Olmesartan, Hypertension, Left ventricular hypertrophy.*

Introduction

Hypertension (high blood pressure) affects approximately 1 billion individuals worldwide. Epidemiological studies show a steadily increasing trend in hypertension prevalence over the last 40 years, more in urban than in the rural

areas. Hypertension is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths in India.[1] Current treatment guidelines recommend that BP should be reduced to <130/80mm Hg in patients with diabetes mellitus or chronic renal disease and to <140/90mm Hg in all others.[2] However, many patients with essential hypertension fail to achieve these targets with currently recommended treatments. Because the treatment of hypertension is among the leading indications for the use of drugs, new agents constantly are being introduced and heavily promoted. The choice of drugs is one of the factors that affects the efficacy of therapy.

At present several Angiotensin receptor blockers (ARBs) are in use for the treatment of hypertension, heart failure and diabetic nephropathy. The newest agent in the class is Olmesartan medoxomil approved by FDA in April 2002 and widely used since then. Thus, by this study we will analyse the clinical outcome of Olmesartan medoxamil in patient with hypertension.

Aims & Objectives

1. To study the change in BP from baseline after giving Olmesartan
2. To study the change in ECG findings from baseline after giving Olmesartan.
3. To study the change in ECHO findings from baseline after giving Olmesartan.

Materials and Methods

The present prospective study was carried out on 39 cases with 18-70 years age group diagnosed as hypertension (stage I and stage II - JNC7)[2] in the district Gwalior (M.P.) and surrounding areas between the year2007-2008. Following cases were excluded in our study:

- Severe hypertension(DBP >110mm Hg or SBP >200mmHg)
- History of secondary hypertension including renal disease, pheochromocytoma, Cushing's disease.
- Pregnant or lactating female.
- History of myocardial infarction (MI), Percutaneous transluminal coronary angiography (PTCA), Coronary artery bypass grafting (CABG), unstable angina pectoris or an episode of heart failure requiring hospitalization.
- Previous history of CVA or TIA.
- History of allergy to Olmesartan medoxomil.
- Any serious disorder, including pulmonary, hepaticrenal, gastrointestinal, uncontrolled endocrine/metabolic hematological/ oncological, neurological, and psychiatric disease that would interfere with the conduct of the study or interpretation of data.
- Diabetes mellitus patients.

After taking written informed consent detail history, demographic and clinical data, including past medical and family history; presenting symptoms and signs; physical examination findings, BP, anthropometric measurement, body mass index, and systemic examination findings were recorded in preformed proformas.

Hematological and Biochemical assessment included hemoglobin, total leukocyte count, ESR, fasting and postprandial blood sugar, blood urea, serum creatinine, serum bilirubin and lipid profile were done and finding noted.

BP will be taken in the upper arm in the patients comfortably seated with the back and arm supported, the leg uncrossed and the upper arm at the level of heart. Presence of hypertension will be defined as per the Joint National Committee (JNC) VII criteria.

Standard 12 lead ECGs will be recorded at 25 mm/s and 0.1 mv/ mm standardization with equipment whose frequency response characteristics met recommendation of American Heart Association. In the ECG Sokolow- Lyon index is calculated (sum of the amplitude of the S wave in in lead V1 and the R wave in lead V5 or V6). If it is equal to or more then 3.5mV then it is considered as positive. If it less than 3.5 mv then it is considered as negative.

2D guided M-mode echocardiogram of Left ventricle at the tip of mitral leaflet using the parasternal view done to measure left ventricular dimension including interventricular septal thickness in diastole (IVSTD), posterior wall thickness in diastole (PWTD) and left ventricular internal diameter at diastole (LVIDD), will be measured from 2D guided M-mode echocardiograms of Left ventricle at the tip of mitral leaflet using the parasternal view.

Olmesartan will be given to the patients with starting dose of 20mg / day, if blood pressure not controlled in follow up period the dose may be increased. All patients will be registered and followed up after a period of 3 month and 6months from the day of registration. At 3 month and 6-month blood pressure, ECG and, left ventricle (LV) dimensions and Left ventricular mass index (LVMI) by Echocardiography will be measured and data will be compared by appropriate statistical tests.

Statistician Analysis

Values are expressed as the Mean+/- standard deviation paired 't' test was used to compare values from the baseline run-in period with values obtained during the treatment period. The level of significance was set at $p<0.05$ for all comparisons.

Results

As shown in table 1, in our study 64.10% cases were male while female are only 35.895% making male: Female ratio is 1.78 which is in favor of male. Maximum number of cases were in the age group 61-75 years (46.15%) followed by age group 46-60 years (41.02%).Main presenting complaint was headache (73.92%) followed by weakness (25.64%) and ghabrahat (23.07%). Duration of hypertension was less than 5 years in 56.41% of cases. Family history of hypertension present in 66.67% cases. History of smoking and tobacco chewing were most common findings (20.51% each) followed by physical inactivity and high salt intake (12.82% each).The 51.28% patients belong to the normal BMI group (18.5-24.9) followed by that of overweight category (38.46%). Amongst male cases 68% were of stage I whereas 32% were of stage II amongst female 64.28% were of stage I and 35.71% were of stage II hypertension.

As described in Table 2 & 3, ECG findings of LVH present in 7.69% of cases with stage II hypertension at baseline which was decreased to 5.55% after three month and 2.81 % after 6 months of giving Olmesartan.

As in table 4, baseline significant LVMI was present in 82.05% cases, they all were of stage II hypertension.

As described in table 5, on comparison between SBP and DBP at baseline and after three months mean reduction was 6.72±7.54 with $P < 0.0001$ and 6.94±6.16 with $P < 0.0001$, after 6 month the mean reduction in SBP was 10.16±9.57 with $P < 0.001$ and 9.38±6.56 with $P < 0.001$.On comparison between mean LVMI at baseline and after 3 months mean reduction was 0.57±1.01 with P=0.12(not significant) after 6 month the mean reduction was 1.93±2.10 with P=0.025 (significant).

Table 1: Distribution of cases according to demographic and clinical profile:

Variables		Male	Female	Total
Sex		25(65.41%)	14(35.89%)	
Age Group	18-30	0 (0%)	0 (0%)	0 (0%)
	31-45	3 (12%)	2 (14.28%)	5 (12.82%)
	46-60	12 (48%)	4 (28.57%)	16 (41.02%)
	61-75	10 (40%)	8 (57.14%)	18 (46.15%)
Presenting Compaints	Headache	18(72%)	12(85.71%)	30 (76.92%)
	Ghabarahat	5(20%)	4(28.71%)	9(23.07%)
	Weakness	5(20%)	5(35.71%)	10(25.64%)
	Easy Fatigue	3(12%)	3(21.42%)	6(15.38%)
	Chest Pain	3(12%)	1(7.14%)	4(10.25%)

	Others	2(8%)	1(7.14%)	3(7.69%)
Past History (Duration)	≤5	14 (56%)	8(57.14%)	22 (56.41%)
	≥5	11 (44%)	6(42.85%)	17(43.58%)
Family History of Hypertension	Present	18(72%)	8 (57.14%)	26(66.67%)
	Absent	5(20%)	6(42.85%)	11(28.20%)
Personal History	SMOKING	8 (32%)	0	8 (20.51%)
	Alcoholic Intake	4 (16%)	0	4 (10.25%)
	Tabacco Chewing	6 (24%)	2 (14.28%)	8 (20.51%)
	Physical Inactivity	4 (16%)	1 (7.14%)	5 (12.82%)
	Physosocial Stress	2 (8%)	1 (7.14%)	3 (7.69%)
	High Salt Intake	3 (12%)	2 (14.28%)	5 (12.82%)
	Not Significant	10 (40%)	8 (57.14%)	18 (46.15%)
BMI	18.5-24.9	15(60%)	5(35.71%)	20(51.28%)
	25-29.9	8(32%)	7(50%)	15(38.46%)
	30-39.9	2(8%)	2(14.28%)	4(10.25%)
stage of hypertension	Stage I	17(68%)	9(64.28%)	26(66.66%)
	Stage II	8(32%)	5(35.71%)	13(33.33%)

Table 2: Distribution of cases according to staging of hypertension and Electrocardiography finding of Left Ventricular Hypertrophy

LVH by ECG	**Stage I (n=26)**				**Stage II (n=13)**				**Total (n=39)**	
	Male(n=17)		Female (n=9)		Male(n=8)		Female (n=5)		No.	%
	No	%	No	%	No	%	No	%		
Present	0	0	0	0	2	25	1	20	3	7.69
Absent	17	100%	9	100%	6	75%	4	80%	36	92.3%

Table 3: Comparison of the number of patients with ECG diagnosed LVH at baseline, 3 month and 6 months after giving Olmesartan

LVH by ECG	**Baseline (n=39)**		**3 Month (n=36)**		**6 Month (n=36)**	
	No	%	No	%	NO	%
Present	3	7.69	2	5.55	1	2.81
Absent	36	92.3	34	94.44	35	97.22

Table 4: Showing comparison of the number of patients with normal or increased left ventricular mass Index, 3 month and 6 months follow up after giving Olmesartan

LVMI	**Baseline (n=39)**		**3 Month (n=36)**		**6 Month (n=36)**	
	No	%	No	%	NO	%
Present	32	82.05	28	77.77	20	55.55
Absent	7	17.94	12	23.22	16	45.45

Table 5: Distribution of cases as per mean systolic blood pressure (SBP), diastolic blood pressure (DBP) echocardiographic left ventricular mass index (LVMI) and statistical analysis of patient during baseline, 3 month and 6 months follow up after giving Olmesartan

Time Interval	**Number of patients**	**Mean±Standard Decviation**		
		SBP mmHg	**DBP mmhg**	**LVMI (Mean±SD)**
Baseline	39	148.66±9.51	91.66±7.53	43.23±25.13
3 months	36	141.94±5.52	84.77±6.94	42.65±24.73
6 months	36	138.50±4.31	82±5.39	41.30±23.61

Discussion

The present study was carried out with aim to study the effects of Angiotensin receptor blocker Olmesartan medoxomil in patients of essential hypertension stage I and stage II as per the JNC VII criteria. As there are several drugs available for the treatment of hypertension the real challenge while choosing antihypertensive lies in

identifying drug therapy that offer desired blood pressure control, with minimum adverse effect and is well tolerated to the patient, so that patients are willing adhere to drug therapy regimen for the long term while maintaining quality of life.

In the present study 64.10% of cases were male with female are only 35.89% the male to female ratio is 1.78 which is in favor of male may be due to increasing smoking and addiction prevalent. In female may be due to hormonal protection up to age of menopause and delay in seeking medical advice we found low rate compare to male.[3] In our study number of cases increased with the increase in age maximum number of patients (48.15%) were in age group 61-75 years. These findings of current study were comparable to the data from the 7th report of joint national committee on hypertension suggested the prevalence of hypertension increases with advancing age to point where more half of people 60-69 years of age and approximately 3-4th of those 70 years of age and older are affected.[2]

In present study main presenting complaint was headache (76.92%), which was similar to various sectional survey. In the study by Steward et al, headache was present in 71% of hypertensive patients who were aware of their diagnosis.[4] Family history of hypertension was present in 66.67% which was consistent with the previous study by Braunwald et.al, in which genetic sharing, genetic contributions have been estimated in the range from 30-60%.[5] In the study of Dominiczac et al the estimate of heritability based on office BPs were in the range of 20% to 40%.[4]

In the present study smoking was found in majority of cases including 20.51%, tobacco chewing found in 20-51%. History of high salt intake and physical inactivity each present in 12.82% of cases. History of alcohol intake was less common as well as history of psychosocial accounting for 10.25% and 7.69% respectively which is supported by different studies including study of Szczech et al, Beard et al and Brydon and Steptoe.[4]

In the present study 32% of male and 50% of female were in the overweight category which was near comparable to the Framingham study in which the incidence of hypertension was increased 46% in men and 75% in women who were overweight, defines as BMI of 25.0 to 29.9 as compared to normal weight persons.[5]

In the present study 66.66% of cases were of stage I and 33.335 of stage II hypertension. Increase number of cases in stage I hypertension may be seeking earlier attention to their medical problems.

In the present study ECG findings of LVH present in 7.69% cases which was comparable to the previous studies of Schmieder & Messerli et al, which showed that LVH is identified by ECG in only 5% to 10% of hypertensive cases.[6] Whereas study by Shine YJ et al ECG for diagnosis of LVH showed sensitivity of 20.0%.[7] In the comparison of this study there were a smaller number of patients in our study with ECG diagnosed LVH. This may be as most of the patients were of stage I hypertension and already on treatment.

In our study at baseline increase in the LVMI was found in the 82.05% of the cases. These data were not comparable to the previous study of Schmieder and Messerli et al, where they found LVH by echocardiography in nearly 30% of unselected hypertension adults.[6] This may due to the effect from the level of blood pressure several other factors like obesity, high dietary sodium intake, alcohol abuse, diabetes, hypercholesterolemia, genotype, polymorphism of the Angiotensin type 2 receptor gene and serum aldosterone levels were responsible for the same. Low sample size and selection of cases from tertiary care Centre was the other reason for difference in opinion.

In our study mean systolic BP at baseline was 148.66+/- mmHg, at 3 months after treatment was 141.94±5.52 mm Hg. The mean reduction was 6.72±7.54 mmHg with p value< 0.0001. Mean SBP at 6 months was 1138.50±4.31 mmHg with mean reduction from baseline after treatment was

10.16±9.57 mmHg with p value< 0.0001. Similarly, the mean DBP at baseline, 3 month and 6 month was 91.66±7.53 mmHg, 84.77±6.94 mmHg and 82±5.36 mmHg respectively with mean reduction at 3 month was 6.94±6 mmHg and at 6 month was 9.38±6.56 mmHg p value < 0.0001 for pair. The reduction in the mean SBP and mean DBP in current study was comparable to results published by Manoria et al. The result of OLMIBEST study showed the mean reduction from baseline in diastolic BP at week 8 was 11.8 mmHg and that in SBP 17.8 mmHg. The study even demonstrated that monotherapy with Olmesartanat the recommended daily dose (20mg) is effective in patients with mild to moderate hypertension.[9] The result of current study were also comparable to the study by Neutel JM et al which was a multi-centre, randomised, placebo-controlled, double-blind clinical trials involving a total of 2,693 subjects from three centers in the US and four center in Europe were reported in a meta-analysis in 2001. The length of treatment in these studies spanned from six to 12 weeks. At the recommended starting those of 20 mg/day, the mean change in DBP and SBP were-12.2 and 15.1 mmHg respectively.[10] Thus, current open level treatment with Olmesartan medoxomil 20mg per day for 6 months confirmed the high antihypertensive efficacy of this regimen in the treatment of essential hypertension.

On comparison between mean LVMI at baseline and after 3 months mean reduction was 0.57±1.01 with p value of 0.12 (not significant) after 6 month the mean reduction was 1.93±2.10 with p value of 0.025 (significant).Previous study by Domenico Galzerano et al on Telmisatan for 44 weeks showed that in Telmisartan-treated patients, LV mass index was reduced by 21.9±5.9 g/m2, which represents a 15.7% reduction. In carvedilol-treated patients, LV mass index was reduced by 12.8±3.5 g/m2, representing a 9.0 % regression and proved that Telmisartan was significantly superior to carvedilol, P< 0001. In our study the mean reduction of LVMI was superior to the study by Domenico Galzerano. This may be because of differences in method of indexing of left ventricular mass in both the studies.[9]

Overall, 4 patients out 39 experienced adverse events including dizziness, headache and upper respiratory tract infections. Most adverse events were mild and were considered unrelated/unlikely related to the medication. Out 39 patients 3 patients were lost in the first follow up.

Conclusion

Olmesartan medoxomil at the recommended dose of 20 mg once daily will be effective in treatment of essential hypertension. These results support the use of this dose regimen in the initial management of hypertensive patients. Olmesartan medoxomil was not effective in regression of ECG based left ventricular hypertrophy in patient of essential hypertension. Olmesartan medoxomil reduce the left ventricular mass index. The reduction in the LVMI was statistically significant.

Funding: No Funding Sources

Conflict of Interest: None Declared

Ethical Approval: The study was approved by the Institutional Ethics Committee

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