

A Comparative Analysis to Determine the Anti-Hypertensive Effect of Olmesartan Medoxomil and Enalapril

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ABSTRACT

Background: The industrial revolution, development and adoption of western life style have made hypertension a significant health problem in India and thus have adversely affected the cardiovascular haemodynamics. Olmesartan medoxomil, a prodrug, is hydrolyzed to olmesartan during absorption from the gastrointestinal tract. Olmesartan is a selective AT1 subtype angiotensin II receptor antagonist. The aim of the present study is to determine the antihypertensive effect of olmesartan medoxomil and enalapril.

Materials and Methods: The present prospective study was conducted in the medicine department of Rajindra Hospital, Patiala. All the patients reporting to the OPD of the department whether new hypertensive or previously suffering from Stage I or Stage II hypertension were included in the study. 50 patients were put on Olmesartan and 50 on Enalapril for the treatment of hypertension. All the data obtained was arranged in a tabulated form and analysed using SPSS software. Student t test was used a test for significance and p value of less than 0.05 was considered significant.

Results: In group A (Olmesartan), 8 patients were in the age group 20-39 years, 24 patients were in the age group 40-59, 15 patients were in the age group 60-79, 3 patients were in the age group ≥ 80 . In group B (Enalapril), 7(14%) patients were in the range of 45-54 kg, 16(32%) kg were in the range of 55-64

kg There was observed marked fall in SBP (mm Hg) with drug therapy in both groups. In group A (Olmesartan), the mean SBP (mm Hg) at the beginning of trial, at 4 weeks and at 8 weeks was 162 ± 6.37 , 152.2 ± 4.63 and 149.16 ± 5.62 respectively and the fall in SBP (mm Hg) with the treatment was statistically significant ($p < 0.05$).

Conclusion: On long term basis both the drugs are equally effective but immediate effect is seen by olmesartan.

Keywords: Hypertension, Haemodynamics, Significant.

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INTRODUCTION

The industrial revolution, development and adoption of western life style have made hypertension a significant health problem in India and thus have adversely affected the cardiovascular haemodynamics. Elevation of systolic blood pressure remains one of the commonest chronic diseases in westernized populations, and is emerging as a major health problem in developing world. Hospital statistics in Delhi reveal that out of all medical admissions, hypertension was present in 3.2% of cases and constituted 21.1% of all cardiovascular disorders.^{1,2} Normal BP with respect to cardiovascular risk is less than 120/80 mmHg. However, unusually low readings should be evaluated for clinical significance. Recent studies using revised criteria BP 140 and /or 90 mm Hg have shown a high prevalence of hypertension among urban adults.³ Maintenance of a normal blood pressure is

dependent on the balance between the cardiac output and peripheral vascular resistance. Most patients with essential hypertension have a normal cardiac output but a raised peripheral resistance. Peripheral resistance is determined not by large arteries or the capillaries but by small arterioles, the walls of which contain smooth muscle cells i.e. peripheral resistance is determined by ratio of lumen to wall thickness as well as neuro humoral influences that act on vascular smooth muscles. Humoral and locally acting substances include prostaglandins and kinins (vasodilators) & angiotensin II (vasoconstrictor) which is active principal in renin angiotensin system. Contraction of smooth muscle cells is thought to be related to a rise in intracellular calcium concentration, which may explain the vasodilatory effect of drugs that block the calcium channels. Prolonged smooth

muscle constriction is thought to induce structural changes with thickening of the arteriolar vessel walls possibly mediated by angiotensin, leading to an irreversible rise in peripheral resistance. Angiotensin II is an extremely potent vasoconstrictor. It also increases release of noradrenaline, reinforcing vasoconstriction and increases the heart rate and force of contraction. Olmesartan medoxomil, a prodrug, is hydrolyzed to olmesartan during absorption from the gastrointestinal tract. Olmesartan is a selective AT1 subtype angiotensin II receptor antagonist. The aim of the present study is to determine the antihypertensive effect of olmesartan medoxomil and enalapril.

MATERIALS AND METHODS

The present prospective study was conducted in the medicine department of Rajindra Hospital, Patiala. All the patients reporting to the OPD of the department whether new hypertensive or previously suffering from Stage I or Stage II hypertension were included in the study. The study included a total of 100 subjects

which were divided into Group A and Group B randomly. Patients with associated LVF, IHD and DM were not included in the study. Pregnant women were also excluded. Patients fulfilling the following requirements prior to recording the BP were included in the study : No caffeine for preceding hour, No smoking for preceding 30 minutes, No exogenous adrenergic stimulants e.g. phenylephrine in nasal decongestants etc. After thorough history, clinical examination and baseline investigations patients were put on drug treatment with Olmesartan and Enalapril. 50 patients were put on Olmesartan and 50 on Enalapril for the treatment of hypertension. Olmesartan was started as 20 mg and Enalapril was started as 5 mg as daily dose in the morning. BP was recorded daily in the morning in the ward patients and weekly in OPD patients. Patients were followed for a duration of 8 weeks. All the data obtained was arranged in a tabulated form and analysed using SPSS software. Student t test was used a test for significance and p value of less than 0.05 was considered significant.

Table 1: Age Distribution

Age Group (Years)	Group A (Olmesartan)		Group B (Enalapril)	
	No. of patients	Percentage	No. of patients	Percentage
20-39	8	16%	5	10%
40-59	24	48%	21	42%
60-79	15	30%	23	46%
≥80	3	6%	1	2%
Total	50	100%	50	100%
Range	29-80		32-80	
Mean ± SD	53.46 ± 13.78		56.40 ± 12.33	
't'	-1.124			
p	>0.05			
Significance	NS			

Table 2: Comparison Of Body Weight (Kg) In Group A (Olmesartan) And Group B (Enalapril)

Body Weight (kg)	Group A (Olmesartan)		Group B (Enalapril)	
	No. Of patients	Percentage	No. Of patients	Percentage
45-54	11	22%	7	14%
55-64	20	40%	16	32%
65-74	13	26%	16	32%
75-84	6	12%	11	22%
Total	50	100%	50	100%
Range	45-84		45-84	
Mean ± SD	63.22 ± 10.25		67.12 ± 11.15	
't'	-1.82			
p	>0.05			
Significance	NS			

Table 3: Comparison of Fall in SBP (mmHg) in Group A (Olmesartan) with Group B (Enalapril) at Different Time Intervals

Periods (weeks)	Group	No. of patients	Mean of difference ± SE	p value
0 – 4	Group A	50	9.76 ± 1.02	< 0.05
	Group B	50	4.48 ± 0.77	(S)
0 – 8	Group A	50	12.84 ± 1.13	> 0.05
	Group B	50	11.80 ± 1.32	(NS)

Table 4: Comparison of fall in DBP (mmHg) in Group A (Olmesartan) with Group B (Enalapril) at Different Time Intervals

Periods (weeks)	Group	No. of patients	Mean of difference ± SE	p value
0 – 4	Group A	50	6.28 ± 0.77	< 0.05
	Group B	50	4.04 ± 0.61	(S)
0 – 8	Group A	50	9.84 ± 0.89	> 0.05
	Group B	50	7.40 ± 0.82	(NS)

RESULTS

A total of 100 subjects were enrolled. Table 1 shows the age distribution in both groups. In group A (Olmesartan), 8 patients were in the age group 20-39 years, 24 patients were in the age group 40-59, 15 patients were in the age group 60-79, 3 patients were in the age group ≥80. In group B (Enalapril), 5 patients were in the age group 20-39 years, 21 patients were in the age group 40-59, 23 patients were in the age group 60-79, 1 patient is in the age group ≥80. On applying student t test there was no significant difference in the age range amongst Group A and Group B as the p value was more than 0.05.

Table 2 shows the comparison of weight (kg) in both groups. In group A (Olmesartan), 11(22%) patients were in the range of 45-54 kg, 20(40%) kg were in the range of 55-64 kg, 13(26%) were in the range of 65-74 kg, 6(12%) were in the range of 75-84 kg. In group B (Enalapril), 7(14%) patients were in the range of 45-54 kg, 16(32%) kg were in the range of 55-64 kg, 16(32%) were in the range of 65-74 kg, 11(22%) were in the range of 75-84 kg. On applying student t test there was no significant difference in the body weight amongst Group A and Group B as the p value was more than 0.05. Table 3 shows the comparison of fall in systolic blood pressure amongst both the groups. There was observed marked fall in SBP (mm Hg) with drug therapy in both groups. In group A (Olmesartan), the mean SBP (mm Hg) at the beginning of trial, at 4 weeks and at 8weeks was 162 ± 6.37, 152.2 ± 4.63 and 149.16 ± 5.62 respectively and the fall in SBP (mm Hg) with the treatment was statistically significant (p <0.05). In group B (Enalapril), the mean SBP (mm Hg) at the beginning of trial, at 4 weeks and at 8weeks was 161.96 ± 5.89, 157.48 ± 7.63, and 150.16 ± 9.63 respectively and the fall in SBP (mm Hg) with the treatment was statistically significant (p <0.05). The mean fall in SBP from 0-4 week interval in Group A and group B was 9.76 ± 1.02 and 4.48 ± 0.77 respectively. There was a significant fall inn SBP in Group A compared to Group B. At 0-8 week interval, there was no significant difference in the fall in SBP amongst both the groups. Table 4 shows the comparison of fall in Diastolic blood pressure amongst both the groups. There was observed marked fall in DBP (mm Hg) with drug therapy in both groups. In group A (Olmesartan), the mean DBP (mm Hg) at the beginning of trial, at 4 weeks and at 8weeks was 101 ± 2.62, 95.52 ± 3.60 and 91.9 ± 4.70respectively and the fall in DBP (mm Hg) with the treatment was statistically significant (p <0.05). In group B (Enalapril), the mean DBP (mm Hg) at the beginning of trial, at 4 weeks and at 8weeks was 99.64 ± 3.82, 95.6 ± 4.00, and 92.24 ± 5.05 respectively and the fall in DBP (mm Hg) with the treatment was statistically significant (p <0.05).The mean fall in DBP from 0-4 week interval in Group A and group B was 6.28 ± 0.77 and 4.04 ± 0.61respectively. There was a significant fall inn DBP in Group A compared to Group B. At 0-8 week interval, there was no significant difference in the fall in DBP amongst both the groups.

DISCUSSION

With changing times, in today’s world of cut throat competition, life has given man so many advanced technologies, facilities and all the gadgets our forefathers could have ever dreamt of. But with this bane, the increasing stress, strain, hurries and worries of life has entrapped man in the vicious circle of certain silent killing diseases; and one of them is hypertension. Hypertension affects approximately 50 million individuals in the United States and approximately 1 billion worldwide. The prevalence of hypertension will even increase further unless broad and effective preventive measures are implemented. The ever increasing introduction of new therapeutic agent means that the potential for drug interaction is likely to escalate. The age in group A (olmesartan) ranged from 29-80 years with a mean age of 53.46 ±13.78 years. Age range in group B (enalapril) was 32-80 years with a mean age of 56.40 ±12.33 years. The age was comparable in the two groups (p>0.05). So there was no significant difference in both age groups as far as the age is concerned. In a similar type of study, Frishman et al (1994) reported mean age of 53 ± 12 years and Lewin et al (1993) reported mean age of 56 ± 1.7 years which was comparable to present study.^{4,5} The mean body weight (kg) in years in group A and B was 63.22 ± 10.25 and 67.12 ± 11.15 respectively. So there was no significant difference in both groups as far as the body weight (kg) is concerned (p>0.05). The antihypertensive effects of Olmesartan medoxomil have been demonstrated in seven placebo-controlled studies at doses ranging from 2.5 mg to 80 mg for 6 to 12 weeks, each showing statistically significant reductions in peak and trough blood pressure. A total of 2693 patients (2145 Olmesartan medoxomil; 548 placebo) with essential hypertension were studied. Olmesartan medoxomil once daily, lowered diastolic and systolic blood pressure. A dose of 20 mg daily of Olmesartan medoxomil produces a trough sitting BP reduction over placebo of about 10/6 mmHg and a dose of 40 mg daily produces a trough sitting BP reduction over placebo of about 12/7 mmHg. Olmesartan medoxomil doses greater than 40 mg had little additional effect. The onset of the antihypertensive effect occurred within 1 week and was largely manifested after 2 weeks (Benicar 2005).⁶ In a number of clinical trials, the agent generally lowered both mean DBP and SBP by at least 10 mmHg after treatment for 8 weeks. Importantly, the majority of patients in clinical trials achieved target DBP of <90 mmHg.^{7,8} After completion of 8 weeks study in group A, administration of olmesartan showed prompt fall in supine SBP from 162 ± 6.37 to 149.16 ± 5.62 mmHg (mean fall 12.84 mmHg), which was statistically significant (p <0.05). The fall in BP was significant till 8 weeks. Oparil S et al (2001) conducted a 8 weeks study with olmesartan 20-40mg, the fall in the mean SBP was 12.5 mmHg and the fall in mean DBP was 8.50 mmHg.⁹ Zabłudowski et al (1988) observed mean reduction in SBP with enalapril by 12 mmHg and DBP by 11 mmHg.¹⁰ In salt-restricted

hypertensive adults, a single dose of olmesartan medoxomil lowered mean 24 hour ambulatory BP and increased renin and angiotensin II concentrations in the plasma.¹¹ Stumpe et al 2002 in a double-blind, randomized, parallel-group study in which 316 patients with mild-to-moderate hypertension (DBP 95–114 mmHg) were treated with either olmesartan medoxomil or losartan for 12 weeks. After 2, 4 and 12 weeks, DBP showed significantly greater reductions with olmesartan medoxomil (8.4 mmHg, 9.1 mmHg, 10.6 mmHg, respectively) than with losartan (6.2 mmHg, 6.4 mmHg, 8.5 mmHg, respectively; 95% confidence index [CI] below zero.¹²

CONCLUSION

On comparing the antihypertensive efficacy, olmesartan produced greater fall in both systolic and diastolic blood pressure at 4 weeks of study, which was statistically significant ($p < 0.05$). But at the end of 8 weeks, both olmesartan and enalapril produced almost similar fall in both systolic and diastolic blood pressure which was statistically non-significant ($p > 0.05$). On long term basis both the drugs are equally effective but immediate effect is seen by olmesartan.

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