Original Research Article

Efficacy and safety of olmesartan and hydrochlorothiazide versus telmisartan and hydrochlorothiazide in newly diagnosed patients with mild-to-moderate hypertension

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Abstract

Background: Hypertension is one of the most prevalent noncommunicable diseases. The Joint National Commission VIII guidelines recommend angiotensin receptor blockers (ARBs) as the first-line drug and addition of hydrochlorothiazide (HCTZ) increases their efficacy. Olmesartan medoxomil is recently introduced, whereas telmisartan is a relatively older ARB. This study was conducted to assess the efficacy and safety of olmesartan and HCTZ versus telmisartan and HCTZ in the treatment of mild-to-moderate hypertension.

Materials and Methods: A total of 120 patients with mild-to-moderate hypertension were recruited and randomized to receive either olmesartan 20 mg+HCTZ 12.5 mg (Group O) or telmisartan 40 mg+HCTZ 12.5 mg (Group T) orally once daily for 8 weeks. Blood pressure (BP) and heart rate were recorded at baseline and at 4th and 8th weeks, but blood sugar and lipid profile were estimated at baseline and 8th week.

Results: Forty-six Group O and 44 Group T patients completed the study. Majority of patients were in the fifth decade of life (72.3%), 56% were males, and 35% had type II diabetes mellitus and received oral antidiabetics. The mean BP was 148.6 ± 5.9/89.2 ± 5.9 and 147.9 ± 5.2/88.1 ± 4.2 mmHg at baseline and decreased significantly at week 8 (131.0 ± 5.4/80.3 ± 2.9 and 136.8 ± 5.5/83.6 ± 3.9 mmHg) in Group O and Group T respectively. Patients in Group O had significant reduction in systolic BP (SBP) ($P = 0.0001$) and diastolic BP ($P = 0.04$) than that in Group T. More than 10 mmHg decrease in SBP was observed in 86.9% versus 65.9% of patients in Group O and Group T, respectively, which was statistically significant ($P = 0.01$). Diabetic patients in both groups had a significant decrease in blood sugar by week 8, but intergroup comparison was insignificant. Change in heart rate and lipid profile was negligible. Common adverse effects were dizziness, abdominal pain, and pedal edema in both groups.

Conclusion: Olmesartan + HCTZ was more effective than telmisartan + HCTZ in lowering BP.

Keywords: Hydrochlorothiazide, hypertension, olmesartan, telmisartan

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INTRODUCTION

According to the WHO statistics, 9.4 million annual deaths were due to raised blood pressure (BP).[1] In India, the prevalence of hypertension is 25% in urban and 10%–15% among rural adults.[2] Complications of hypertension include, stroke, coronary artery disease, and chronic kidney disease. The

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Joint National Committee (JNC) VIII guidelines recommend the use of angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers (ARBs), thiazide diuretics, or calcium channel blockers as initial drugs for the treatment of hypertension.[3] The synergistic action of two antihypertensive drugs from different classes has been shown to benefit patients profoundly, in terms of effective reduction in BP and minimizing the side effects due to each individual drug. Olmesartan medoxomil is recently introduced, whereas telmisartan is a well-established ARB. Our aim was to compare a fixed-dose combination of olmesartan + hydrochlorothiazide (HCTZ) and telmisartan + HCTZ, in terms of efficacy and safety in hypertensive patients.

MATERIALS AND METHODS

This study was conducted after obtaining approval from the Institutional Ethics Committee (No. DMC/KLR/UDOME/IEC-CER/148). Duration of the study was 1½ years. Patients of either gender, aged between 30 and 70 years, and newly diagnosed with mild-to-moderate hypertension (JNC VIII) were recruited. Patients with both hypertension and diabetes mellitus (type II) were included if they were on oral antidiabetic drugs. Exclusion criteria were patients with severe hypertension, renal or hepatic dysfunction, and pregnant and lactating women. The patients satisfying the inclusion criteria and willing to give written informed consent were randomized to receive either olmesartan 20 mg + HCTZ 12.5 mg (Group O) or telmisartan 40 mg + HCTZ 12.5 mg (Group T), orally once daily for 8 weeks. BP and heart rate were recorded at baseline and at 4th and 8th weeks. Laboratory investigations such as fasting blood sugar (FBS), postprandial blood sugar (PPBS), lipid profile, and serum electrolytes were assessed at baseline and repeated at the end of 8th week. The patients were advised to report any adverse events as and when they occurred and these were documented and assessed in accordance with the WHO causality assessment scale.

Statistical analysis

Taking into consideration a power of 80% and an α error of 5% to detect a difference of 3.2 mmHg in the diastolic BP (DBP) at 8 weeks, with an effect size of 0.64 and a dropout rate of 10%, the sample size was calculated to be 42 patients per group. The demographic data were analyzed using descriptive statistics. The BP values of the two groups were compared using unpaired *t*-test, paired *t*-test, and repeated-measures ANOVA. The FBS, PPBS, lipid profile, and serum electrolytes were compared using the unpaired *t*-test. Adverse effects were analyzed using the Chi-square test. $P < 0.05$ was considered statistically significant.

RESULTS

Participants recruited in our study were 120, but 90 participants completed the 8-week study period [Figure 1]. Analysis was done for patients who have completed the study. Majority of patients in both groups were males (56%) and there was family history of hypertension in 11 and 13 patients in Groups O and T, respectively. Headache and dizziness were the most common presenting symptoms. Most patients in Group O and Group T (65.2 and 56.8%, respectively) were asymptomatic. Demographic characteristics [Table 1] and laboratory investigations were comparable between the groups at baseline.

In comparison to the baseline, there was significant reduction in both systolic BP (SBP) and DBP at the end of 4th and 8th weeks in both the treatment groups [Figures 2 and 3]. Eight weeks after therapy with olmesartan + HCTZ and telmisartan + HCTZ, the number of patients who had a decrease of more than 10 mmHg in SBP (40 vs. 29; $P = 0.017$) and 5 mmHg in DBP (34 vs. 23; $P = 0.028$) compared to baseline with respective combination was assessed and the percentage of patients was significantly more with olmesartan + HCTZ [Figure 4]. There was a significant decrease in both FBS and PPBS at week 8 in those receiving olmesartan + HCTZ; however, only PPBS reduced with telmisartan + HCTZ [Table 2]. There was no statistical significance when these parameters were compared between the groups (FBS: $P = 0.069$; PPBS: $P = 0.674$).

Subgroup analysis of hypertensives with diabetes who were on treatment and received study medication had

Table 1: Demographic data at baseline

	Group O (olmesartan + HCTZ)	Group T (telmisartan + HCTZ)	*P*
Number of patients	46	44	-
Mean age (years)	53.6±8.8	53.1±8.5	0.770
Gender (male/female)	26/20	25/19	0.573
Patients with Type II diabetes mellitus (%)	15 (34.0)	18 (39.1)	0.666
Clinical symptoms of hypertension present (%)	15 (32.6)	19 (43.1)	0.385
SBP (mmHg)	148.6±5.9	147.9±5.2	0.583
DBP (mmHg)	89.2±5.9	88.1±4.2	0.329
Baseline HR (beats/min)	78.0±7.4	77.4±5.5	0.672

Values: Mean±SD. SD: Standard deviation, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HR: Heart rate, HCTZ: Hydrochlorothiazide

significant reduction in both FBS and PPBS at week 8 compared to baseline [Table 3]. The decrease was greater in those receiving olmesartan + HCTZ; however, intergroup comparison was not significant (FBS: P =0.056; PPBS: P = 0.224). There was no significant difference between baseline and end of the study within and between the two groups in lipid profile and serum electrolytes.

The most common adverse effects were dizziness, pedal edema, and gastrointestinal intolerance and were graded "possible" in majority of patients, according to the WHO causality assessment scale. Both drug combinations were well tolerated and had a comparable safety profile.

DISCUSSION

In India, cardiovascular diseases account for 1.5 million deaths yearly and by 2020, it is predicted to be the leading cause of morbidity and mortality.[4,5] Hypertension is a major risk factor for the development of cardiovascular disease. Increase in SBP and DBP increases the risk of stroke, coronary artery disease, myocardial infarction,

Table 2: Blood sugar values at baseline and week 8

	Group O (*n*=46)			Group T (*n*=44)		
	Baseline	8 weeks	*P*	Baseline	8 weeks	*P*
FBS (mg/dl)	121.5±31.6	111.5±16.0*	0.006	110.9±24.3	110.0±27.2	0.772
PPBS (mg/dl)	186.6±45.5	168.3±25.3*	0.008	191.4±51.4	170.7±27.6#	0.001

FBS: Fasting blood sugar, PPBS: Postprandial blood sugar

Table 3: Blood sugar levels in hypertensive patients with diabetes

Olmesartan and HCTZ (*n*=15)				Telmisartan and HCTZ (*n*=18)		
Mg/dl	Baseline	8th week	*P*	Baseline	8th week	*P*
FBS, mean±SD	136.7±25.8	119.6±14.1	0.01	146.1±26.1	130.3±16.5	0.02
PPBS, mean±SD	190.4±44.9	163.4±27.4	0.04	195.4±46.3	175.8±29.7	0.04

HCTZ: Hydrochlorothiazide, FBS: Fasting blood sugar, PPBS: Postprandial blood sugar, SD: Standard deviation

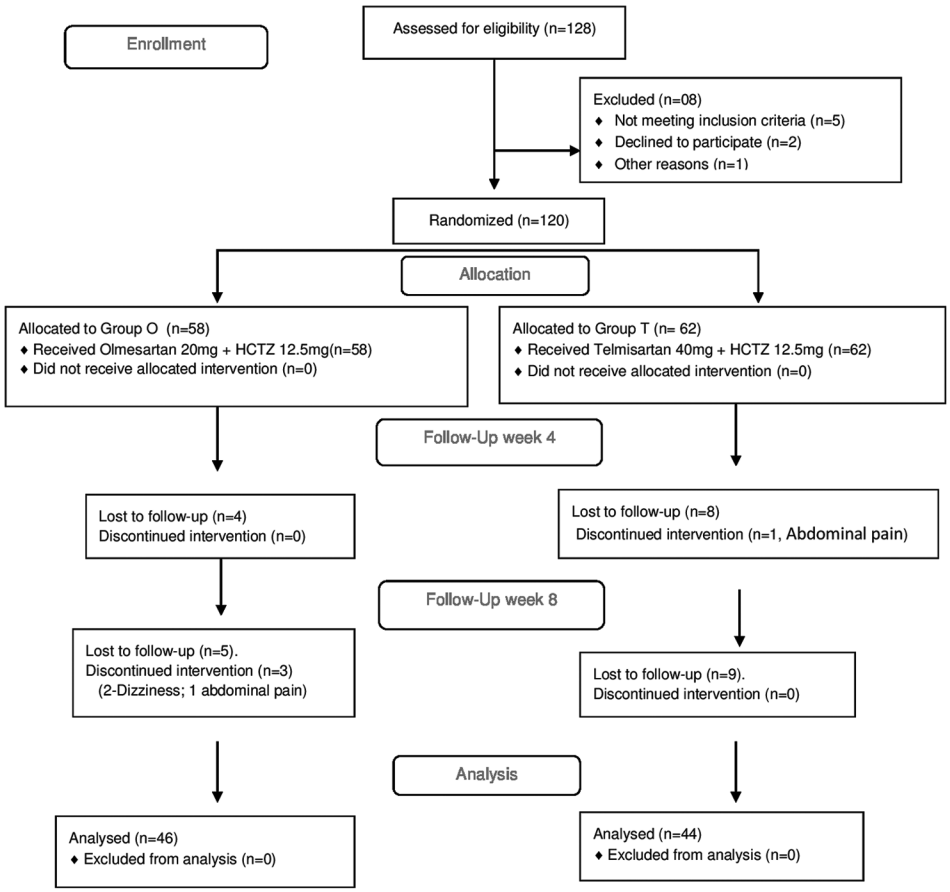

Figure 1: Consort flow chart representing recruitment, randomization, and follow-up

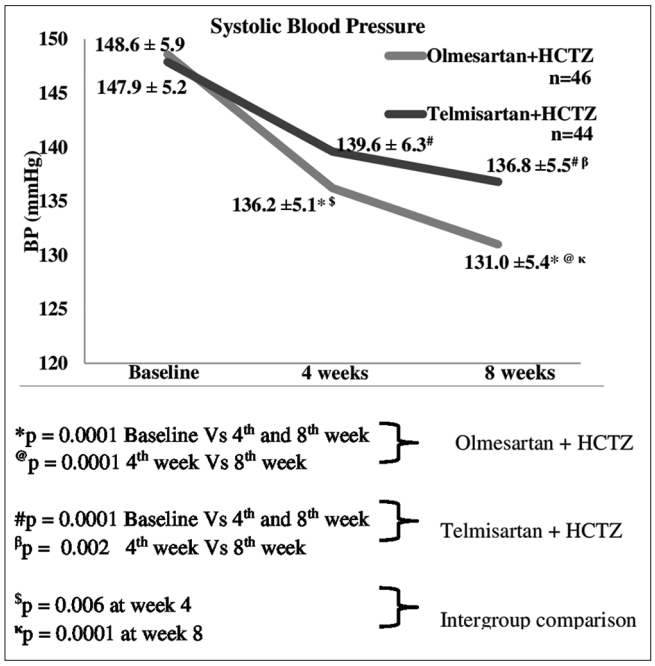

Figure 2: Comparison of systolic blood pressure within and between the groups

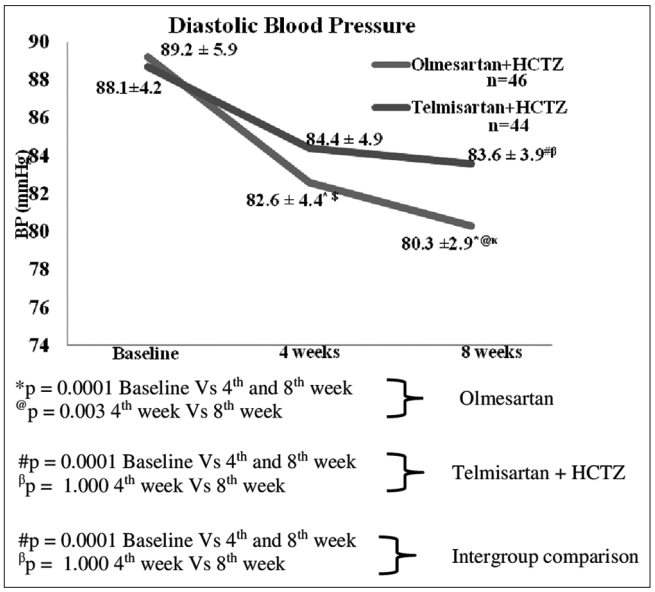

Figure 3: Comparison of diastolic blood pressure within and between the groups

cardiac failure, and renal disease. Prevalence rates of hypertension in India are 29%–45% and 25%–38% in men and women, respectively.[6,7] ARBs antagonize the activity of angiotensin II and reduce proteinuria, improve renal function, and attenuate the fibrotic component of left ventricular hypertrophy; therefore, they not only control hypertension, but also prevent cardiorenal diseases.[8] These drugs are especially useful in patients having comorbid conditions such as diabetes mellitus and chronic kidney disease.

In the present study, 120 patients newly diagnosed with hypertension were randomized and received either olmesartan + HCTZ or telmisartan + HCTZ [Figure 1], in which ninety patients completed the 8-week study period. The demographic characteristics were comparable. Most patients were in the fifth decade of life (72.3%). An epidemiological study by Parikh *et al.* showed that 65.2% of people between 51 and 60 years of age suffer from hypertension.[7] We observed that more than 56% of patients were asymptomatic, the diagnosis of hypertension in these patients was thus incidental. The time lapse between the onset of hypertension and its diagnosis is delayed due to its silent nature and this may lead to complications which are largely avertible by timely intervention.[8,9] In our study, the most common complaints among symptomatic patients were headache and dizziness. Type II diabetes mellitus was seen in 34% and 39% of our patients in Groups O and T, respectively. According to the Hong Kong Cardiovascular Risk Factor Prevalence Study, 44% of hypertensives had impaired glucose tolerance.[10] Studies show that there is a significant overlap in the etiopathogenesis of these two diseases, evidenced by the influence of sympathetic nervous system, renin-angiotensin-aldosterone system, oxidative stress, and adipokines that bring about inflammation and worsen atherosclerosis.[11-16]

We observed that after initiation of therapy with the study medications, patients with initial complaints had symptomatic relief. There was significant reduction in SBP and DBP compared to baseline at 4th and 8th weeks in both groups. Intergroup comparison at the 4th week showed that there was a statistically significant difference in SBP but not in DBP, whereas at the 8th week, this significant difference was observed with both BPs [Figures 2 and 3]. It has also been proven that a 5–6 mmHg reduction in DBP reduces the risk of stroke and coronary artery disease by 38% and 16%, respectively.[17] In this context, it can be established that the relationship between elevation in BP and adverse cardiovascular outcome is linear and every mmHg reduction offers better prognosis. In the present study, majority of patients in both groups experienced >10 mmHg reduction in SBP and >5 mmHg reduction in DBP . Intergroup comparison revealed that this number was significant in those receiving olmesartan + HCTZ. Thus, this combination is more efficacious than telmisartan + HCTZ in lowering BP.

It has been shown that both olmesartan and telmisartan improve glycemic control by increasing insulin sensitivity, hence we studied their effect on FBS and PPBS.[18,19] In the present study, FBS decreased significantly by week 8

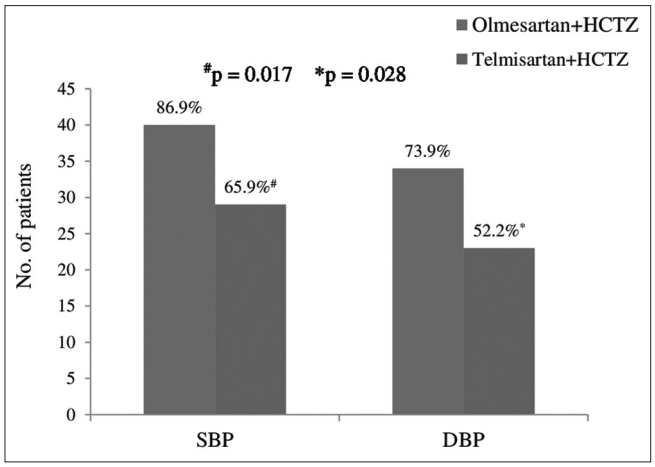

Figure 4: Number of patients with >10 mmHg decrease in systolic blood pressure and >5 mmHg in diastolic blood pressure from baseline to week 8 between the groups

in patients receiving olmesartan + HCTZ, but PPBS levels decreased with both drugs. Subgroup analysis of diabetic patients in our study showed a reduction in FBS and PPBS in both groups at the second follow-up visit, compared to baseline [Table 3]. Intergroup comparison of these parameters in all patients who completed the study and also subgroup analysis of diabetic patients between the two drugs were not significant.

We did not observe a substantial change in the lipid profile of patients in both treatment groups. It is likely that a higher dose or longer duration of therapy may be required to observe such effects. The number of adverse effects was slightly higher in patients receiving olmesartan + HCTZ. Dizziness, pedal edema, and gastrointestinal intolerance were most common and as per WHO causality assessment scale, the reaction was "possible" in a majority of patients. These events were mild to moderate and subsided on continuation of therapy. As per the results of Daiichi-Sankyo-Integrated Summary of Safety, headache, dizziness, and vertigo occurred most frequently with both drugs, and only 6% of events are reported as severe.[20] Our findings are consistent with the existing literature and both treatment groups are found to be well tolerated by patients and hence have a similar safety profile. Three patients receiving olmesartan + HCTZ and one patient receiving telmisartan + HCTZ had adverse effects and subsequently dropped out of the study.

Limitation

Long-term follow-up would have helped us to establish the effects on lipid profile and also determine which combination delayed the onset of coronary artery disease, myocardial infarction, cardiac failure, stroke, and renal disease.

CONCLUSION

In our study, we observed that olmesartan + HCTZ produced a greater reduction in both SBP and DBP than telmisartan + HCTZ and both combinations had comparable safety profile, hence olmesartan + HCTZ is more efficacious in the treatment of hypertension.

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Conflicts of interest

There are no conflicts of interest.

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