Internet Journal of Medical Update

Original Work

Randomized, interventional, prospective, comparative study to evaluate the antihypertensive efficacy and tolerability of ramipril versus telmisartan in stage 1 hypertensive patients with diabetes mellitus

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ABSTRACT: Angiotensin converting enzyme inhibitors and angiotensin receptor blockers are keystones for therapy of hypertension in diabetes because they show favourable effects on diabetic nephropathy and cardiovascular disease outcomes. A prospective, randomized, interventional clinical study of one year duration was conducted to comparatively evaluate anti-hypertensive efficacy and tolerability profile of ramipril versus telmisartan in stage 1 hypertensive patients associated with type 2 diabetes mellitus, amongst patients of either sex attending the medicine OPD of Rohilkhand Medical College and Hospital, Bareilly. Clearance from institutional ethical committee and written informed consent of the participants was taken. The enrolled 222 patients were randomized into ramipril and telmisartan groups, of these only 192 patients completed the study. The data obtained were statistically analyzed by paired and unpaired t-test using SPSS software. Prevalence of hypertension in diabetics was more in 41 to 50 years age group, in females (male: female ratio= 0.92:1) and in rural areas (rural: urban ratio= 0.61:1). Baseline BP values were equally matched in both groups. The SBP and DBP were reduced from baseline in all the ten follow-ups and were statistically significant (p <0.0001 for both groups). Regarding adverse effects, both drugs were well tolerated though dry irritating cough and dizziness was more in ramipril group. Both ramipril and telmisartan as monotherapy were equally effective in lowering SBP and DBP on prolonged use in diabetic hypertensives but the incidence of adverse effects was higher with ramipril hence telmisartan be preferred.

KEY WORDS: *Ramipril; Telmisartan; Systolic; Diastolic blood pressure; Stage 1 hypertensive patients; Diabetes mellitus*

INTRODUCTION

Hypertension is a multifactorial disease affecting one billion people worldwide. It is the most common, readily identifiable and a reversible risk factor for myocardial infarction, stroke, heart failure, atrial fibrillation, aortic dissection and peripheral arterial disease[1]. Currently, high blood pressure causes about 54% of stroke and 47% of ischemic heart disease worldwide[2]. Thus, high blood pressure remains the leading cause of death worldwide and one of the world's great public health problems[1]. As with smoking, diabetes, and dyslipidemia, hypertension is an important risk factor for cardiovascular diseases, which are responsible for roughly 30% of deaths worldwide[3]. Hypertension is an extremely common co-morbid condition in diabetes, affecting 20-60% patients.

The renin-angiotensin-aldosterone system (RAAS) plays an important role in the pathogenesis of atherosclerosis and pathophysiology of cardiovascular disease. Angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) have become keystones of therapy for hypertension in diabetes because of their broadly demonstrated favourable effects on diabetic nephropathy and cardiovascular disease outcomes, as well as their modest favourable effects on measures of glucose metabolism[4].

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The aim of the present study is to comparatively evaluate the anti-hypertensive efficacy of Ramipril versus Telmisartan in stage 1 hypertensive patients (JNC VII) associated with type 2 diabetes mellitus as well as their tolerability and adverse effects profile.

METHODOLOGY

A prospective randomized interventional, open label, comparative clinical study of one year duration (Jan 2013 to Jan 2014) was conducted amongst patients aged 30 to 80 years, of either sex attending the medicine outdoor patient department of Rohilkhand Medical College and Hospital, Bareilly, diagnosed as hypertension (JNC VII stage 1) associated with type 2 diabetes mellitus.

Both newly diagnosed patients and those who had discontinued antihypertensive medication voluntarily for more than 4 weeks comprised the study population. Inclusion criteria were both male and female patients between 30 to 80 years of age with type 2 diabetes and stage 1 hypertension (JNC VII). A total of 222 eligible patients who conformed to inclusion criteria were enrolled and were allotted a study number sequentially. All the odd study numbers were allotted to ramipril group and even study numbers to telmisartan group respectively. 111 patients were allotted each to ramipril group and telmisartan group.The ramipril treated group received RAMIPRESS 5 mg (Cipla) and the telmisartan treated group received CRESAR 40 mg (Cipla). Doses of anti-hypertensive agents were fixed throughout the study period and no upward titration of doses was done. Written informed consent from all the participants was undertaken before starting the study and the participants were free to withdraw without prejudice at any time. The study protocol was approved by the institutional ethical committee.

Patients on other anti-hypertensive therapy, patients of secondary hypertension, symptomatic heart failure, significant valvular heart disease, pericardial constriction or effusion, congenital heart disease, syncope episodes of unknown etiology, uncontrolled hypertension (BP > 160/100 mm Hg), pregnant, lactating and child bearing females, females on oral contraceptives, significant renal disease; serum creatinine> 2 mg/dl, significant liver disease; SGOT/SGPT > 2 times the normal values, known hypersensitivity to ACE inhibitors or ARBs, inability to tolerate ramipril or telmisartan, or use of steroid or NSAIDs were excluded from the study. 30 patients who did not turn up for regular follow up or whose compliance was irregular were excluded from the study. Thus, only 192 patients

(98 in ramipril group and 94 in telmisartan group) completed the study and were finally evaluated statistically.

The demographic informations viz. name, age, sex, and nativity and also information about social and cultural factors, and educational status were recorded based on structured pretested and predesigned questionnaire. All the recruited subjects underwent a detailed physical examination inclusive of routine investigations and for the assessment of hypertensive and diabetic complaints, if any. Special investigations were done in limited number of patients as per need. At baseline and each visit blood pressure was recorded with an appropriate sized cuff in the right arm in seated position with the back supported at heart level after patients had taken a rest for 15 minutes. Measurement of the subject's blood pressure was recorded by standardized calibrated mercury column type sphygmomanometer and stethoscope. Blood pressure was also recorded in standing and lying positions to rule out any autonomic neuropathy. Two readings were taken 5 minutes apart and the mean was recorded as clinic blood pressure.

Enrolled patients under treatment were subsequently monitored, investigated and reassessed at regular intervals for a total duration of nine months. Further at each visit, the patients were queried for objective and subjective systemic adverse effect of the drugs. The subjective symptoms such as headache, dizziness, fatigue, back pain, dyspepsia, myalgia, pruritus, nausea, dry cough were assessed by questioning the patient at each visit. Adverse effects following therapy, if any, were noted down for both regimens.

For type 2 diabetes either metformin (500 mg) once or twice daily was used or else a combination of metformin (500 mg) and glimepride (1 mg) once or twice daily was administered to achieve adequate glycemic control of blood sugar.

The data obtained were statistically analyzed by paired and unpaired t-test using SPSS software version 17.5 and Microsoft Office Excel 2007; p-value < 0.05 was taken as significant.

RESULT

Table 1 shows a higher prevalence of hypertension in females 115 (52%) as compared to males 107 (48%). Male: female ratio was 0.92:1. A larger number of patients belonged to rural areas 138 (62%) as compared to urban areas 84 (38%). The urban: rural ratio was 0.61:1.

Table 1: Distribution of male and female in rural and urban population

Groups	Rural		Urban		Total
	M	F	M	F	
Ramipril	31	37	26	17	111
Telmisartan	30	40	20	21	111
Total	61	77	46	38	222

M=male, F=female

Table 2 depicts that maximum incidence 41% of hypertensives with type 2 diabetes mellitus was noted in the age group of 41-50 years, followed by less than 40 years age group, 25% and minimum incidence of 5% was observed in elderly patients of the age group 71-80 years. Educational status-wise, 77 (35%) patients were illiterates. Graduates, post graduates or professionals together comprised 21% of the patients

Table 3 shows a decreasing trend in the mean values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) at each follow up visit in all the 98 hypertensive patients with type 2 diabetes mellitus following ramipril therapy. The first follow up (FU) was done at two weeks and the subsequent follow ups were done at one month interval each and the BP values compared with the baseline blood pressure. The SBP and DBP changes between baseline and subsequent follow-up visits showed statistically significant consistent reduction (p < 0.0001).

Table 4 shows a similar decreasing trend in the mean values of SBP and DBP at each follow up visit in hypertensive patients with type 2 diabetes mellitus following telmisartan therapy. Similar to

ramipril the follow ups were done initially at two weeks and then every month for the nine months study period. The comparative SBP and DBP values between baseline and the subsequent follow-up visits showed statistically significant consistent reduction (p < 0.0001) amongst the enrolled 94 patients.

Table 5 shows the baseline blood pressure values were almost similar in both the groups that is SBP was 152.08±6.04 and 151.8±5.56 mm Hg in ramipril and telmisartan groups respectively and DBP was 88.59±8.34 and 87.78±7.92 mm Hg in ramipril and telmisartan group respectively. The mean SBP and mean DBP were thus comparable between the two groups. It was observed that SBP was significantly reduced after nine months therapy by 42.6 mm Hg in the ramipril group, and by 42.5 mm Hg in the telmisartan group (p < 0.0001 for both groups). However, the difference in the mean reduction of SBP between the two groups was not statistically significant (p > 0.05). Further, DBP was significantly reduced by 17.69 mm Hg in the ramipril group and by 16.81 mm Hg in the telmisartan group (p < 0.0001 for both groups). However, the difference in the mean reduction of DBP between the two groups was not statistically significant (p > 0.05).

Table 6 shows no statistically significant increase in serum creatinine, blood urea and SGPT but a statistically significant increase in serum potassium levels with both ramipril and telmisartan therapy. There was a minimal decrease in serum total cholesterol (not significant) and in serum LDL (statistically significant) in both groups. There was an increase in serum HDL which was statistically significant in both groups. Regarding serum triglycerides, there was statistically significant increase, but within normal range in ramipril group as compared to telmisartan group where the increase was statistically not significant.

Table 2: Age distribution and educational status of patients

Age (Yrs)	Groups		Total No. (%)	Educational Status	Groups		Total No. (%)
	Ramipril	Telmisartan			Rami	Telmi	
Upto 40	29	26	55 (25%)	**Ill**	41	36	77 (35%)
41-50	42	49	91 (41%)	**≤HS**	22	32	54 (24%)
51-60	22	24	46 (21%)	**≤ I**	21	23	44 (20%)
61-70	10	9	19 (8%)	**G**	15	10	25 (11%)
71-80	8	3	11 (5%)	**PG**	12	10	22 (10%)
Total	111	111	222 (100%)	**Total**	111	111	222 (100%)

Ill=Illeterate; HS=High School; I=Intermediate; G=Graduate; PG=Postgraduate

Table 3: Comparative follow up values of SBP and DBP with Ramipril (n=98)

Systolic Blood Pressure				Diastolic Blood Pressure			
MEAN SBP±SD	FU SBP±SD	t-value	p-value	MEAN DBP±SD	FU DBP±SD	t-value	p-value
152.08±6	137.26±7.7 1st FU (2 weeks)	18.763	< 0.0001	88.59±8.3	83.95±7.5 1st FU (2 weeks)	5.66	< 0.0001
152.08±6	131.22±4.5 2nd FU (1 month)	33.13	< 0.0001	88.59±8.3	79.95±5.2 2nd FU (1 month)	9.2	< 0.0001
152.08±6	127.04±3.2 3rd FU (2 months)	39.315	< 0.0001	88.59±8.3	79.08±5.4 3rd FU (2 months)	10.53	< 0.0001
152.08±6	124.34±3.0 4th FU (3 months)	41.68	< 0.0001	88.59±8.3	76.73±3.5 4th FU (3 months)	12.31	< 0.0001
152.08±6	121.02±2.7 5th FU (4 months)	42.63	< 0.0001	88.59±8.3	76.89±7.3 5th FU (4 months)	10.55	< 0.0001
152.08±6	117.6±2.0 6th FU (5 months)	53.47	< 0.0001	88.59±8.3	76.33±2.4 6th FU (5 months)	13.49	< 0.0001
152.08±6	116.85±1.8 7th FU (6 months)	53.31	< 0.0001	88.59±8.3	76.25±2.6 7th FU (6 months)	13.91	< 0.0001
152.08±6	112.89±1.1 8th FU (7 months)	63.9	< 0.0001	88.59±8.3	72.79±1.1 8th FU (7 months)	19.06	< 0.0001
152.08±6	111±1.0 9th FU (8 months)	65.03	< 0.0001	88.59±8.3	70.06±0.3 9th FU (8 months)	22	< 0.0001
152.08±6	109.48±9.2 10th FU (9 months)	66.5	< 0.0001	88.59±8.3	70.90±1.0 10th FU (9 months)	20.53	< 0.0001

FU – Follow up

Table 4: Comparative follow up values of SBP and DBP with Telmisartan (n=94)

Systolic Blood Pressure				Diastolic Blood Pressure			
MEAN SBP±SD	FU SBP±SD	t-value	p-value	MEAN DBP±SD	FU DBP±SD	t-value	p-value
151.8±5.5	136.59±6.8 1st FU (2 weeks)	20.97	< 0.0001	87.78±7.9	84.55±7.0 1st FU (2 weeks)	3.79	< 0.0001
151.8±5.5	130.89±3.9 2nd FU (1 month)	41.72	< 0.0001	87.78±7.9	79.93±5.0 2nd FU (1 month)	8.42	< 0.0001
151.8±5.5	126.59±3.5 3rd FU (2 months)	42.19	< 0.0001	87.78±7.9	79.55±4.5 3rd FU (2 months)	8.65	< 0.0001
151.8±5.5	124.32±2.9 4th FU (3 months)	48.31	< 0.0001	87.78±7.9	77.04±3.7 4th FU (3 months)	11.93	< 0.0001
151.8±5.5	120.89±2.7 5th FU (4 months)	47.67	< 0.0001	87.78±7.9	77.82±1.7 5th FU (4 months)	11.58	< 0.0001
151.8±5.5	117.44±2.3 6th FU (5 months)	56.45	< 0.0001	87.78±7.9	76.23±2.5 6th FU (5 months)	13.18	< 0.0001
151.8±5.5	116.63±2.0 7th FU (6 months)	58.47	< 0.0001	87.78±7.9	76.14±2.7 7th FU (6 months)	13.13	< 0.0001
151.8±5.5	112.82±1.2 8th FU (7 months)	66.66	< 0.0001	87.78±7.9	72.74±1.5 8th FU (7 months)	18.20	< 0.0001
151.8±5.5	110.95±1.0 9th FU (8 months)	68.87	< 0.0001	87.78±7.9	70.06±0.5 9th FU (8 months)	21.54	< 0.0001
151.8±5.5	109.55±0.8 10th FU (9 months)	72.21	< 0.0001	87.78±7.9	70.97±1.00 10th FU (9 months)	20.43	< 0.0001

FU – Follow up

Table 5:Comparative reduction of SBP & DBP between baseline & at end of treatment in both regimens

	Systolic Blood Pressure			Diastolic Blood Pressure		
	Ramipril	**Telmisartan**	**DIFF**	**Ramipril**	**Telmisartan**	**DIFF**
Baseline	152.08±6.04	151.8±5.56	0.28	88.59±8.34	87.78±7.92	0.81
At10th Follow-up	109.48±0.925	109.55±0.8375	-0.07	70.90±1.001	70.97±1.001	-0.07
Reduction from Baseline	- 42.6 95%CI (41.29 to 43.83)	- 42.25 95% CI (41.09 to43.42)	0.35	- 17.69 95%CI (16 to19.42)	- 16.81 95% CI (15.18 to 18.44)	0.88
P-value	< 0.0001	< 0.0001	>0.05	< 0.0001	< 0.0001	>0.05

CI = Confidence Interval, DIFF = Difference

Table 6:Effect on laboratory parameters with Ramipril and Telmisartan

Lab	Ramipril				Telmisartan			
	Baseline Mean±SD	After 10th FU Mean±SD	T-value	P-value	Baseline Mean±SD	After 10th FU Mean±SD	T-value	P-value
CRE	1.0023 ±0.2	1.0082 ±0.2	0.18	0.87	1.0049 ±0.2	1.0122 ±0.2	0.30	0.77
URE	29.86 ±6.5	29.37 ±4.9	0.65	0.52	30.10 ±6.2	29.34 ±5.3	0.94	0.35
POT	4.414 ±0.2	4.556 ±0.3	4.31	<0.0001	4.415 ±0.2	4.555 ±0.3	4.33	<0.0001
SGPT	30.63 ±5.8	30.93 ±6.3	1.08	0.28	34.44 ±4.9	34.29 ±4.5	0.26	0.79
CHO	213.08 ±29.1	210.84 ±24	0.58	0.56	219.90 ±21.8	210.18 ±25.1	2.70	0.008
TG	114.63 ±13.3	123.23 ±8	5.63	<0.0001	120.05 ±10.1	123.86 ±7.8	3.12	0.002
LDL	141.37 ±13.1	128.7 ±5.6	8.57	<0.0001	143.64 ±13.4	128.38 ±5.4	9.74	<0.0001
HDL	41.39 ±4.8	44.85 ±3.1	5.94	<0.0001	41.20 ±4.7	44.48 ±5	4.49	<0.0001

CRE = S. Creatinine, POT = S. Potassium, CHO = S. Cholesterol, TG = S. Triglyceride, URE = B. Urea

Table 7 depicts adverse effects, which were noted in 15 patients of ramipril group and 6 patients in telmisartan group. Hypotension, hyperkalemia and angioedema were not observed in either ramipril or telmisartan group.

Table 7:Adverse effects in Ramipril and Telmisartan

Adverse Effects	Ramipril	Telmisartan
	No. (%)	**No. (%)**
Dry Cough	6 (0.06%)	1 (0.01%)
Dizziness	3 (0.03%)	1 (0.01%)
Headache	3 (0.03%)	3 (0.03%)
GI Upset	3 (0.03%)	1 (0.01%)

DISCUSSION

Hypertension and diabetes mellitus are both highly prevalent, chronic, incurable ailments requiring continuous, regular and palliative therapy almost throughout the life of the individual. These clinical conditions thus require continuous monitoring to prevent various complications as well as progression of the disease. Hence, proper optimal therapy is a must to achieve treatment goals as suggested by the latest guidelines.

Although a wide variety of antihypertensive agents belonging to different pharmacological classes targeting different physiological components are being prescribed for the management of hypertension, yet therapy with renin-angiotensin system blockers has been chosen for comparative evaluation as these two agents namely, ACE

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inhibitor (ramipril) and ARB (telmisartan) in doses applied cause minimum adverse effects profile and are better tolerated as well as these two agents are quite effective in Asian populations.

The present study comprised of 222 newly diagnosed hypertensive patients conforming to JNC VII stage 1 criterion[5] with type 2 diabetes mellitus who have reported to the medicine outpatient department of Rohilkhand medical college and hospital, Bareilly. The patients were randomized in two groups (ramipril group and telmisartan group) to carry out non-interventional, observational study and they received therapy with either ramipril 5 mg once daily, or telmisartan 40 mg once daily. The two groups were well balanced with regards to initial SBP and DBP for comparative evaluation.

A total of 30 patients dropped out of the study period (13 from ramipril and 17 from telmisartan group) and they were not considered while computing the results as well as for the statistical analysis. The dropouts are probably due to the higher cost of the drugs because the subject has to take both antihypertensive as well as antidiabetic agents simultaneously almost throughout life, lack of compliance, adverse effects as well as poor awareness that despite their blood pressure being controlled, they have to take the drugs almost throughout life. Also some enrolled patients have to be dropped out due to augmentation in therapy with two or more drugs for hypertension.

Treatment adherence is an important issue for the therapy of chronic diseases such as hypertension and diabetes. An improvement in adherence is expected to result in better long-term clinical outcomes, including reduced cardiovascular and renal morbidity/mortality. Monotherapy with once daily administration is not only convenient but also improves treatment adherence and compliance. In the present study monotherapy with ramipril or telmisartan has been used and in none of the cases was an upward titration of the dose required. Further, previous studies have shown that telmisartan effectively reduces blood pressure when used alone[6,7]. In a large cohort of patients in Italy, the rate of discontinuation of the initial single antihypertensive drug treatment was lower for ARBs compared with ACE inhibitors (hazard ratio [HR] of 0.92 and 95% confidence interval [CI] of 0.90-0.94)[8]. Although worldwide guidelines recommend combination therapy as first line treatment option for hypertension likely not to be controlled on monotherapy (e.g. 20/10 mm of Hg above target BP)[9,10].

In the present study the M:F ratio is 0.92:1 (107/115). The incidence of gender involvement in hypertension is in conformity with observations reported in serial epidemiological study conducted in Jaipur by Gupta *et al*[11] where the prevalence of hypertension has been reported lower 30% and 36% respectively amongst males as compared to

34% and 38% respectively in females. An earlier study carried out at this centre by Shaifali *et al*[12] has also mentioned a similar M:F ratio of 0.92:1. Further in a study conducted at Jaipur in the year 2002, hypertension was present in 200 males (36.4%) and 215 females (37.5%), and diabetes was found in 72 males (13.1%) and 65 females (11.3%) of the randomly selected adults of more than 20 years of age[11]. Among rural adults, Bansal et *al*[13] have observed that 110/396 (27.8%) female test subjects have hypertension compared to 93/302 (30.9%) male hypertensives; thus their observations contradicted ours.

The prevalence of hypertension in India has increased in both urban and rural subjects. In the present study, the prevalence of hypertension has been found to be higher in rural areas 138 (62%) as compared to urban areas 84 (38%). The urban:rural ratio is 0.61:1. A larger involvement of rural adults has been probably due to a higher stress ratio amongst rural adults owing to poverty, unemployment and decreasing deployment of workers in farm related activities and higher cost of living to meet their livelihood. Moreover, in the present study the catchment population is more from a rural background. Contrasting observations have been reported by Shaifali *et al*[12], Chadha *et al*[14] Hypertension study group[15] and Gupta *et al*[16] who reported a larger involvement of the urban population. Further, review of epidemiological studies also suggests that the prevalence of hypertension is more in urban adults (25%) as compared to rural adults (10-15%). Midha *et al*[17] have reported the prevalence of hypertension in urban adults to be 40.8% and in rural adults to be 17.9%. The highest prevalence of hypertension in rural adults has been reported as 35.9% by Bhardwaj *et al*[18] in Himachal Pradesh and 32.3% by Bansal *et al*[13] in a village of Uttarakhand.

Regarding distribution of patients as per age, the present study has observed a rising trend of hypertension with type II diabetes with increasing age. This observation is in line with Dubey *et al*[19] and Bansal *et al*[13]. Majority of the patients in our study are in the age group of 41-50 years followed by upto 40 years age group. Shaifali *et al*[12] have also reported the highest incidence of hypertension in the age group of 41-50 years age. Dubey *et al*[19] reported the highest incidence of hypertension in the age group of 41 to 60 years 44% (275/623), followed by 30 to 40 years 31% (193/623).These authors have also observed that age, education, lifestyle and socioeconomic status are significantly associated with hypertension.

A rising trend in hypertension with increasing age is consistent with the other studies namely Mehan *et al*[20] in Assam, Deshmukh *et al*[21] in Wardha and Prasanath *et al*[22] in South India. Probably a higher incidence of dyslipidemia as observed in hypertension and diabetes together with rising

atherosclerotic changes in the vascular system with increasing age may account for an increased prevalence of hypertension with increasing age. Moreover, diabetes mellitus is associated with increased oxidative stress due to hyperglycaemia, which together with dyslipidemia is associated with an excess of cardiovascular risk. Also, there are other factors contributing to a rising trend of hypertension like increased life expectancy, urbanization and its attendant lifestyle changes including increased salt intake, increased awareness and increased detection, and increased stressful working hours.

Regarding association of educational status with incidence of hypertension and diabetes mellitus, it is observed that incidence of hypertension is more in illiterate subjects (35%) and less in graduates (11%) and postgraduate/professionals (10%). This is probably due to a larger chunk of patients reporting to our outpatient department being from the rural population, who are primarily illiterate. Again, stressful living conditions and poverty are the prime precipitating causes. In conformity to our observations, Dubey *et al*[19] have observed that people with higher education suffer less from hypertension as compared to those who are less educated. Shaifali *et al*[12] have also observed involvement of only 19.6% graduates and post graduates/professionals with hypertension. In contrast, Chadha *et al*[14] reported a higher incidence of hypertension in the literate population. We cannot definitely comment on the impact of greater awareness, early detection and lifestyle changes regarding incidence of hypertension and diabetes in these groups because of lesser number of postgraduates/professionals in our study. According to Pandit *et al*[23], literacy was a significant independent predictor of blood pressure control.

In our study, the baseline blood pressure values were almost equally matched in both the groups. SBP was 152.08±6.04 mm Hg and 151.8±5.56 mm Hg and DBP was 88.59±8.34 mm Hg and 87.78±7.92 mm Hg in ramipril and telmisartan groups respectively. The mean SBP and mean DBP were thus comparable between the two groups. Other workers[24-26] in the field have also reported a similar baseline value of SBP and DBP. The SBP and DBP reductions from baseline in all the ten follow-up visits have shown statistically significant, regular and consistent reduction (p <0.0001) amongst all 98 patients of ramipril group and in 94 patients of telmisartan group. SBP was significantly reduced after nine months therapy by 42.6 mm Hg in the ramipril group and by 42.25 mm Hg in the telmisartan group (p < 0.0001 for both groups). DBP was also significantly reduced after nine months therapy by 17.69 mm Hg in the ramipril group and by 16.81 mm Hg in the telmisartan group (p < 0.0001 for both groups).

Thus, our findings are qualitatively and quantitatively similar to observations reported by HOPE investigators[24] and ONTAGET investigators[27].

A comparative assessment of changes in SBP with the two regimens showed that there was no statistically significant difference (p-value > 0.05) in SBP reduction. Similarly, a comparison of changes in DBP with the two regimens showed no statistically significant difference (p-value > 0.05) in DBP reduction. The fall in DBP has been noted even at the first follow-up at two weeks. Our observations in respect to DBP are in line with the reports of previous studies[24-26]. Thus, it can be stated that ramipril causes fall in SBP as well as DBP and that the fall in BP may be noted as early as two weeks of therapy. It has been observed that telmisartan, similar to ramipril, has also caused a reduction in SBP and DBP even at the first follow-up at two weeks. Thus, telmisartan is also quite effective in reducing both systolic and diastolic blood pressure in hypertensive patients with type II diabetes mellitus. A decreasing trend in mean values of SBP and DBP at each follow-up is in line with observations of other workers in the field. Owing to long-lasting BP control and CV protection, telmisartan has been identified as a gold-standard treatment and has been recommended as a preferred ARB treatment option.[28]

In summary both ramipril and telmisartan cause decrease in SBP and DBP and the onset of action is within two weeks. We have not observed a greater fall in DBP with telmisartan as has been reported by other workers[27] probably because the doses used in our study were fairly low; rather, there has been a lesser decrease in DBP with telmisartan as compared to ramipril. It is reasonable to express that both the agents caused a regular statistically significant fall in blood pressure and that these agents are equally effective as is reflected by the fact that there is no statistically significant difference (p-value >0.05) between values of blood pressure achieved by the two agents in different follow-ups.

We have recorded only office blood pressure, hence we cannot comment on the observations made by other workers that ARBs, in particular telmisartan, provide superior BP lowering to ACE inhibitors in the early morning as well as in the 24-hour, morning, daytime and night-time periods[26,29]. Several studies have established the superiority of telmisartan compared with other ARBs regarding 24-hour blood pressure lowering efficacy, particularly in the early morning period. Further telmisartan 80 mg had a significantly higher smoothness index than the ARBs losartan and valsartan and the ACE inhibitor, ramipril, and was comparable with amlodipine[30].

Guidelines have recommended more aggressive antihypertensive treatment in diabetes, aiming at values less than 130 mm Hg systolic and 80 mm Hg diastolic. However, the additional beneficial effects of such lower BP targets remain unproven. In a short term (12 weeks) randomized, comparative, study between telmisartan versus ramipril in essential hypertension, Soni *et al*[31] observed that telmisartan (40mg once daily) is as effective as ramipril (10mg once daily) in lowering SBP but produces a greater reduction in DBP than ramipril. It has been observed that both ramipril and telmisartan have fairly good tolerability and adverse effects have been noted in 0.15% in case of ramipril and 0.8% in case of telmisartan. Regarding the tolerability of telmisartan, we have observed that it has an excellent tolerability profile. ARBs have superior tolerability over ACE inhibitors, which inhibit the degradation of bradykinin, leading to adverse effects, such as dry cough and angioedema[32].

Biochemical parameters, showed no statistically significant changes in serum creatinine, blood urea and SGPT with the two regimens. Both ramipril and telmisartan caused an increase in serum potassium levels from baseline which though statistically significant varied within normal range with the continued therapy of 9 months with both these agents. This suggests that caution should be applied on prolonged use.

In the present study, in ramipril group there has been statistically significant increase in serum TG levels though within normal range. This finding has been in line with Schnack *et al*[33] who used ramipril in the dose of 2.5 to 5 mg/day. On the other hand, in telmisartan treated group a statistically non-significant increase in TG has been observed. This observation is in contrast to findings of Inoue *et al*[34] who have reported significant reductions in triglycerides with telmisartan therapy. Further, both ramipril and telmisartan have caused statistically significant reduction in serum LDL and an increase in serum HDL again within normal range; however there has been no statistically significant decrease in total cholesterol values.

It is of interest to mention that workers in the field have observed that elevated non-fasting TG level, which indicate the presence of remnant lipoprotein which are associated with increased risk of MI, IHD and total death in men and women in the general population[35]. Besides, increased TG levels are associated with decreased HDL cholesterol, a strong risk factor for IHD. Moreover, an increased TG levels is a risk factor for cardiovascular disease independent of HDL levels[36]. Since, in our study, neither ramipril nor telmisartan have caused significant alterations in lipid profile beyond the normal values hence, both drugs should be considered safe.

Regarding adverse effects, both the drugs were well tolerated though there were instances of dry irritating cough in six subjects of ramipril group as compared to one in telmisartan group and three subjects each complained of dizziness and GI upset in ramipril group as compared to one each in telmisartan group. Comparatively, telmisartan has caused lesser incidence of adverse effects. There was no incidence of hypotension, hyperkalemia, angioedema or any other major adverse events requiring hospitalization.

In conclusion, comparative evaluation has shown that both ramipril and telmisartan are equally effective in lowering systolic as well as diastolic blood pressure. It has been observed that monotherapy with once daily administration of either agents is quite efficacious in case of stage I hypertensive with diabetes mellitus. Regarding the biochemical parameters, these two agents do not cause a significant effect on lipid profile except that a few lipid parameters have changed though within the normal range. Both the agents have caused increase in serum potassium on long term use and this too is within the upper limits of normal range. Significantly, the incidence of dry cough and dizziness has been more with ramipril, while the incidence of these adverse effects with telmisartan is fairly low. Hence, telmisartan has a better tolerability profile as compared to ramipril.

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