Research Article

Study of changes in serum lipid profile and blood sugar level by perindopril and telmisartan during treatment of systemic hypertension

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ABSTRACT

Background: This study was designed to compare adverse effects on serum lipid profile and blood sugar level in the treatment with two commonly used drugs perindopril and telmisartan in cases of hypertension. This was an "observational" and "cross-sectional" study.

Methods: A total of 100 patients were included in each, Groups A and B. In both groups, half the patients were given perindopril 4 mg OD and half were given telmisartan 40 mg OD for 24 weeks. Total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides (TG), fasting blood sugar (FBS), and postprandial blood sugar (PPBS) level was estimated initially and then at 4th, 12th, and 24th week. Statistical analysis was done using ANOVA.

Results: With perindopril initial means of TC, HDL, LDL, TGs, FBS, and PPBS in Groups A and B were 190.32, 49.76, 117.96, 165.04, 84.56, 122.60, and 188.80, 51.64, 118.52, 159.12, 93.92, 133.60, respectively. After 24 weeks, these values were 190.84, 50.68, 118.60, 163.84, 83.48, 120.20, and 190.96, 52.04, 118.28, 157.56, 93.96, 133.68, respectively ($p > 0.05$). With telmisartan, initial means of TC, HDL, LDL, TG, FBS, and PPBS in both groups were 188.08, 49.76, 118.84, 167.20, 83.72, 120.68, and 188.08, 46.88, 121.96, 167.84, 91.44, 131.72, respectively. After 24 weeks, these values in both groups were 189.36, 49.80, 120.04, 165.96, 82.60, 118.36 and 186.12, 45.28, 121.08, 167.72, 92.76, 129.56 respectively ($p > 0.05$).

Conclusions: It concluded that both perindopril and telmisartan had not any significant adverse effects on plasma lipid profile and blood sugar level in both groups.

Keywords: Perindopril, Telmisartan, Hypertension, Serum lipid profile, Blood sugar level

INTRODUCTION

Systemic arterial hypertension is a condition that affects almost 1 billion people worldwide (2008) and is a leading cause of morbidity and mortality.[1,2] This disease is sometimes called the silent killer.[3] The disease in the majority of the cases is asymptomatic until the damaging effect of hypertension, such as stroke, myocardial infarction, renal dysfunction, visual problem, etc. are observed.[4] In 90-95% of patients, the cause of hypertension is unknown, which is called primary or essential hypertension.[5] The remaining 5-10% of patients has hypertension that secondarily results from some other disorder e.g. renal disease, endocrine disease, or other identifiable cause.

Angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARBs) has been a major therapeutic advance in the management of hypertensive patients.[6] Perindopril is a non-sulfhydryl ACEI approved and extensively studied, highly effective in lowering both systolic and diastolic blood pressure.[7] Telmisartan is an ARBs, it blocks the action of angiotensin at AT-1 receptor in vascular smooth muscle and adrenal gland causing the fall in blood pressure.

This study is being undertaken to compare the effects of perindopril and telmisartan on serum lipid profile and blood sugar level in the treatment of hypertension.

METHODS

This study was done in the Department of Pharmacology and Medicine, Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna. The study protocol was approved by IGIMS Institutional Ethics Committee. Written informed consent was taken from patients during their enrolment for

study. The patient related data, medical history, diagnosis, laboratory values and given treatment were noted in a case record form. This study was done between months of December 2011 to November 2012, for a period of 12 months.

Number of patients included in this study was 200. Patients were included according as per previous study.[8,9]

Source: patients attended outpatient department (OPD) of general medicine and cardiology and admitted in a different unit of Department of Medicine of IGIMS, Patna.

Inclusion criteria

Patient selected for the study were:
1. Adult patients (>18 years of age) of both sexes
2. Newly diagnosed hypertensive patients (patients aged 18 years and older with a blood pressure ≥140/90 mm Hg, with a diagnosis of hypertension seen within a 12 month period and not prescribed any antihypertensive medications) and old hypertensive patients (patients aged 18 years and older with a blood pressure ≥140/90 mm Hg, with diagnosis of hypertension seen for more than 12 months period and prescribed 2 or more anti-hypertensive medications)
3. Range of blood pressure in the study group ≥140/90 mm Hg and ≤180/110 mm Hg.

Exclusion criteria

1. Patient with known sensitivity to ACE inhibitor or ARB
2. Pregnant and lactating women
3. Patient with H/O angioedema
4. Patient with hepatic impairment
5. Patient with renal impairment
6. Patient with acute illness or blood pressure >180 mm Hg systolic or >110 mm Hg diastolic.

Methodology

- Patients were divided into two groups
- Group A - Newly diagnosed patients (100)
- Group B - Old but poorly controlled hypertensive patients (100).

Patients were selected from OPDs of General Medicine and Cardiology units of Department of Medicine of IGIMS, Patna. It is a non-randomized open-label study. In this study, 135 patients were enrolled in Group A, out of which 105 patients completed the therapy. In Group B, 210 patients were enrolled out of which 120 patients completed the therapy.

In both groups, half the patients were given perindopril 4 mg OD and half were given telmisartan 40 mg OD for 24 weeks. If blood pressure was not controlled, dose was titrated according to response and the dose was increased to keep mean arterial pressure between 90 and 115 mmHg after

4th week of treatment. The adjusted dose was kept constant in both groups. Adjusted dose was 8 mg OD for perindopril and 80 mg OD for telmisartan.[10]

Following investigations were done during treatment.
A. Plasma lipid profile
  1. Total cholesterol (TC)
  2. High density lipoprotein (HDL)
  3. Low density lipoprotein (LDL) and
  4. Triglycerides (TG).
B. Blood sugar level
  1. Fasting blood sugar (FBS) level and
  2. Postprandial blood sugar (PPBS) level.

These investigations were performed initially before starting treatment and repeated after 4th, 12th, and 24th week after starting treatment.

RESULTS

Table 1 shows that mean baseline values of TC, HDL, LDL, and TG in both groups of patients were 190.32, 49.76, 117.96, and 165.04. These values after the study period were 190.84, 50.68, 118.60, and 163.84.

Table 2 shows that mean baseline values of TC, HDL, LDL, and TG in both groups of patients are 188.80, 51.64, 118.52, and 159.12. These values after the study period were 190.96, 52.04, 118.28, and 157.56.

In both Tables 1 and 2, p value was >0.05. This means that there was no significant effect of perindopril on serum lipid profile in this study.

Table 3 shows that mean baseline values of TC, HDL, LDL, and TG in both groups of patients were 188.08, 49.76, 118.84, and 167.20. These values after the study period were 189.36, 49.80, 120.04, and 165.96.

Table 4 shows that mean baseline values of TC, HDL, LDL, and TG in both groups of patients were 188.06, 46.88, 121.96, and 167.84. These values after the study period were 186.12, 45.28, 121.08, and 167.72.

Using standard statistical methods, in both the Tables 3 and 4, p value was >0.05. So in this study, telmisartan had no significant effect on lipid profile in both these group of patients.

As shown in Table 5, the mean baseline values of fasting and PPBS were 84.56 and 122.60 in newly diagnosed patients (Group A). After treatment, these values were 83.48 and 120.20.

As shown in Table 6, the mean baseline values of fasting and PPBS were 93.92 and 133.62 in old hypertensive patients (Group B). After treatment, these values were 93.96 and 133.68.

Table 1: Observation of the effect of perindopril on serum lipid profile in Group A patients.

	Total cholesterol					HDL				
	Mean	±SD	±SEM	t value	p value	Mean	±SD	±SEM	t value	p value
Initial	190.32	6.54	1.31	–	–	49.76	3.10	0.62	–	–
4th week	188.34	7.10	1.29	0.60	>0.05	52.78	3.08	0.58	1.85	>0.05
12th week	192.48	6.57	1.35	0.52	>0.05	50.22	2.76	0.55	1.89	>0.05
24th week	190.84	6.69	1.34	0.54	>0.05	50.68	2.84	0.57	1.87	>0.05
	LDL					Triglyceride				
	Mean	±SD	±SEM	t value	p value	Mean	±SD	±SEM	t value	p value
Initial	117.96	5.26	1.05	–	–	165.04	8.44	1.69	–	–
4th week	119.92	5.72	1.09	1.01	>0.05	162.08	9.07	1.72	1.05	>0.05
12th week	117.86	6.31	1.43	1.10	>0.05	164.78	8.45	1.82	1.22	>0.05
24th week	118.60	6.71	1.34	1.00	>0.05	163.84	9.01	1.80	1.15	>0.05

HDL: High density lipoprotein, LDL: Low density lipoprotein, SD: Standard deviation, SEM: Standard error of the mean

Table 2: Observation of the effect of perindopril on serum lipid profile in Group B patients.

	Total cholesterol					HDL				
	Mean	±SD	±SEM	t value	p value	Mean	±SD	±SEM	t value	p value
Initial	188.80	7.99	1.80	–	–	51.64	2.58	0.52	–	–
4 week	186.72	8.83	1.93	0.79	>0.05	58.62	2.98	0.64	0.43	>0.05
12th week	192.96	8.42	2.10	0.86	>0.05	49.98	3.12	0.68	0.46	>0.05
24th week	190.96	10.4	2.08	0.85	>0.05	52.04	3.32	0.66	0.45	>0.05
	LDL					Triglyceride				
	Mean	±SD	±SEM	t value	p value	Mean	±SD	±SEM	t value	p value
Initial	118.52	5.77	1.15	–	–	159.12	10.95	2.19	–	–
4 week	119.52	5.70	1.07	0.17	>0.05	160.12	9.98	2.09	0.87	>0.05
12th week	120.60	5.06	1.05	0.18	>0.05	164.78	9.68	1.76	0.90	>0.05
24th week	118.28	5.08	1.02	0.17	>0.05	157.56	8.92	1.78	0.89	>0.05

HDL: High density lipoprotein, LDL: Low density lipoprotein, SD: Standard deviation, SEM: Standard error of the mean

Table 3: Observation of the effect of telmisartan on serum lipid profile in Group A patients.

	Total cholesterol					HDL				
	Mean	±SD	±SEM	t value	p value	Mean	±SD	±SEM	t value	p value
Initial	188.08	6.36	1.27	–	–	49.76	3.10	0.62	–	–
4th week	190.90	6.16	1.28	0.87	>0.05	50.76	3.17	0.64	0.052	>0.05
12th week	186.78	6.36	1.42	0.81	>0.05	51.80	3.11	0.66	0.053	>0.05
24th week	189.36	6.98	1.40	0.84	>0.05	49.80	3.16	0.63	0.057	>0.05
	LDL					Triglyceride				
	Mean	±SD	±SEM	t value	p value	Mean	±SD	±SEM	t value	p value
Initial	118.84	8.22	1.24	–	–	167.20	10.14	2.03	–	–
4th week	120.86	6.86	1.38	1.42	>0.05	168.70	9.98	2.23	0.98	>0.05
12th week	119.96	6.44	1.58	1.50	>0.05	166.00	10.19	2.05	0.95	>0.05
24th week	120.04	7.84	1.57	1.44	>0.05	165.96	11.68	2.34	0.93	>0.05

HDL: High density lipoprotein, LDL: Low density lipoprotein, SD: Standard deviation, SEM: Standard error of the mean

The p value was >0.05 in both these group of patients for both fasting and PPBS level. This showed that there was no significant effect of perindopril on fasting or PPBS level in both group of patients.

As shown in Table 7, the mean baseline values for fasting and PPBS level in newly diagnosed cases (Group A) were 83.72 and 120.68. After treatment, these values were 82.60, 118.36.

As shown in Table 8, the mean baseline values of fasting and PPBS were 91.44 and 131.72 in old hypertensive patients (Group B). After treatment, these values were 92.76 and 129.56.

P value was >0.05 in both Tables 7 and 8. Hence, there was no significant effect of telmisartan on fasting or PPBS level in both these group.

DISCUSSION

Perindopril is an effective antihypertensive agent with an acceptable side-effect profile in patients of hypertension.[11] Treatment with perindopril has no adverse effects on plasma lipid metabolism, glucose homeostasis, and insulin sensitivity.[12] No significant changes were observed in creatinine clearance, and it was concluded that perindopril

Table 4: Observation of the effect of telmisartan on serum lipid profile in Group B patients.

	Total cholesterol					HDL				
	Mean	±SD	±SEM	t value	p value	Mean	±SD	±SEM	t value	p value
Initial	188.08	9.07	1.81	–	–	46.88	8.60	1.72	–	–
4th week	187.80	7.82	1.56	1.05	>0.05	44.87	7.53	1.67	1.72	>0.05
12th week	190.86	8.73	1.34	1.11	>0.05	43.28	8.11	1.44	1.65	>0.05
24th week	186.12	6.11	1.22	1.06	>0.05	45.28	7.45	1.49	1.68	>0.05
	LDL					Triglyceride				
	Mean	±SD	±SEM	t value	p value	Mean	±SD	±SEM	t value	p value
Initial	121.96	12.13	2.43	–	–	167.84	11.87	2.37	–	–
4th week	120.82	10.11	2.52	0.49	>0.05	168.28	10.82	2.57	0.032	>0.05
12th week	119.76	10.17	2.32	0.51	>0.05	169.55	94.11	3.13	0.034	>0.05
24th week	121.08	11.63	2.33	0.48	>0.05	167.72	15.16	3.03	0.036	>0.05

HDL: High density lipoprotein, LDL: Low density lipoprotein, SD: Standard deviation, SEM: Standard error of the mean

Table 5: Observation of the effect of perindopril on fasting and post prandial blood sugar level in Group A patients.

	FBS					PPBS				
	Mean	±SD	±SEM	t value	p value	Mean	±SD	±SEM	t value	p value
Initial	84.56	9.03	1.81	–	–	122.60	10.36	2.07	–	–
4th week	85.82	8.52	1.62	0.44	>0.05	120.88	9.87	1.98	1.53	>0.05
12th week	87.76	7.96	1.53	0.49	>0.05	124.56	9.28	1.87	1.40	>0.05
24th week	83.48	7.33	1.47	0.45	>0.05	120.20	8.45	1.69	1.49	>0.05

SD: Standard deviation, SEM: Standard error of the mean, FBS: Fasting blood sugar, PPBS: Postprandial blood sugar

Table 6: Observation of the effect of perindopril on fasting and post prandial blood sugar level in Group B patients.

	FBS					PPBS				
	Mean	±SD	±SEM	t value	p value	Mean	±SD	±SEM	t value	p value
Initial	93.92	19.04	3.81	–	–	133.60	21.15	4.23	–	–
4th week	92.80	18.72	4.02	0.64	>0.05	132.80	20.88	3.72	0.68	>0.05
12th week	90.72	18.90	3.52	0.69	>0.05	130.68	21.28	4.05	0.75	>0.05
24th week	93.96	17.86	3.57	0.73	>0.05	133.68	19.39	3.88	0.73	>0.05

SD: Standard deviation, SEM: Standard error of the mean, FBS: Fasting blood sugar, PPBS: Postprandial blood sugar

Table 7: Observation of the effect of telmisartan on fasting and post prandial blood sugar level in Group A patients.

	FBS					PPBS				
	Mean	±SD	±SEM	t value	p value	Mean	±SD	±SEM	t value	p value
Initial	83.72	9.05	1.81	–	–	120.68	10.56	2.11	–	–
4th week	84.56	8.09	1.68	0.72	>0.05	122.80	10.22	2.05	1.62	>0.05
12th week	85.28	7.28	1.69	0.60	>0.05	124.60	9.78	1.88	1.78	>0.05
24th week	82.60	7.40	1.48	0.68	>0.05	118.36	9.89	1.98	1.66	>0.05

SD: Standard deviation, SEM: Standard error of the mean, FBS: Fasting blood sugar, PPBS: Postprandial blood sugar

Table 8: Observation of the effect of telmisartan on fasting and post prandial blood sugar level in Group B patients.

	FBS					PPBS				
	Mean	±SD	±SEM	t value	p value	Mean	±SD	±SEM	t value	p value
Initial	91.44	14.72	2.85	–	–	131.72	21.61	4.32	–	–
4th week	88.28	13.88	2.88	1.05	>0.05	130.82	19.81	4.82	1.16	>0.05
12th week	93.66	14.08	3.12	0.98	>0.05	132.76	22.05	4.16	1.32	>0.05
24th week	92.76	12.55	2.51	1.03	>0.05	129.56	20.13	4.03	1.28	>0.05

SD: Standard deviation, SEM: Standard error of the mean, FBS: Fasting blood sugar, PPBS: Postprandial blood sugar

normalizes blood pressure without affecting glycemic control or renal function.[13] Full-dose RAAS inhibition, particularly with perindopril, effectively reduces BP, improves arterial structure and regulates cardiovascular risk factors in overweight or obese patients with hypertension.[14] Other study it was observed that perindopril showed no significant change in any of metabolic parameters such as a lipid profile, glucose tolerance, body weight or BMI and the drug was well-tolerated and creatinine clearance was unaltered by treatment.[15]

The statistical test used for analysis was ANOVA

With treatment with perindopril mean baseline systolic and diastolic blood pressure in new and old hypertensive group were 166.80, 169.04 and 95.36, 96.08, respectively. After the study period, these values were 118.72, 119.12 and 81.52, 78.50, respectively (p < 0.05). With treatment with telmisartan mean baseline systolic and diastolic blood pressure in new and old hypertensive group were 170.48, 170.00 and 98.96, 95.84, respectively. After the study period, these values were 118.64, 120.00 and 78.96, 88.16, respectively (p < 0.05).

The effect of perindopril on serum lipid profile is shown in Tables 1 and 2. This shows that mean baseline values of TC, HDL, LDL, and TGs in Groups A and B were 190.32, 49.76, 117.96, 165.04 and 188.80, 51.64, 118.52, 159.12, respectively. After 24 weeks values of TC, HDL, LDL, and TGs in Groups A and B were 190.84, 50.68, 118.60, 163.84 and 190.96, 52.04, 118.28, 157.56, respectively. The p value of this study was >0.05. This failed to show any significant effect on serum lipid profile in either newly diagnosed (Group A) or old hypertensive patients (Group B).

The effect of perindopril on blood sugar level is shown in Tables 5 and 6. This showed that mean baseline values of FBS and PPBS in Groups A and B were 84.56, 122.60 and 93.92, 133.60, respectively. After 24 weeks, values of FBS and PPBS in Groups A and B were 83.48, 120.20 and 93.96, 133.68, respectively. The p value in both these group of patients is >0.05 for both fasting and PPBS level. This shows that there is no significant effect on fasting or PPBS level in both groups of patients.

A study observed that telmisartan 40 mg once daily was effective and well-tolerated in the treatment of mild to moderate hypertension.[16] The on target trial was done to compare the efficacy of telmisartan with an ACE inhibitor

enalapril. This study showed that both drugs produced comparable reduction in blood pressure in a broad range of patients with hypertension. Telmisartan appeared to have a better tolerability profile. TEES study was done to compare the efficacy of telmisartan and enalapril and was concluded that telmisartan is well-tolerated and at least as effective as enalapril in treating elderly patients with mild to moderate hypertension.[17] Preclinical and clinical studies indicated that the administration of telmisartan can improve carbohydrate and lipid metabolism without causing the side-effects that accompany full peroxisome proliferator-activated receptor gamma activators. If the preliminary data are supported by the results of ongoing large-scale clinical studies, telmisartan could have a central role in the prevention and treatment of metabolic syndrome, diabetes and atherosclerosis.[18] In a study, data indicated that in insulin-resistant persons 12 weeks of telmisartan result in a significant improvement in glucose metabolism with a predominant improvement in beta-cell function.[19]

Tables 3 and 4 show the effect of telmisartan on serum lipid profile in newly diagnosed (Group A) and old hypertensive (Group B) patients, respectively. Initial means of TC, HDL, LDL, TG in both Groups A and B were 188.08, 49.76, 118.84, 167.20 and 188.08, 46.88, 121.96, 167.84, respectively. After 24 weeks, means of TC, HDL, LDL, TG in both groups were 189.36, 49.80, 120.04, 165.96 and 186.12, 45.28, 121.08, 167.72, respectively. The p value was >0.05. This failed to show any significant effect of telmisartan on serum lipid profile in either newly diagnosed (Group A) or old hypertensive (Group B) patients.

Tables 7 and 8 show the effect of telmisartan on blood sugar level in newly diagnosed (Group A) and old hypertensive (Group B) patients, respectively. Initial means of FBS and PPBS in Groups A and B were 83.72, 120.68 and 91.44, 131.72, respectively. After 24 weeks, means of FBS and PPBS in Groups A and B were 82.60, 118.36 and 92.76, 129.56, respectively. The p value was >0.05. This failed to show any significant effect of telmisartan on blood sugar level in either newly diagnosed (Group A) or old hypertensive (Group B) patients.

CONCLUSION

It may be concluded that ACE inhibitor perindopril and ARB telmisartan both significantly reduces systolic, diastolic

and mean arterial pressure without any significant adverse effect on serum lipid profile and blood sugar level. Their antihypertensive effects were almost equal and comparable. Study should be done on the larger population to substantiate these observations.

ACKNOWLEDGMENTS

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