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Original Article

Pharmacology Section

Study of Changes in Renal Function by Perindopril and Telmisartan during Treatment of Systemic Hypertension

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ABSTRACT

Background: Angiotensin Converting Enzyme Inhibitors (ACEI) and Angiotensin Receptor Blockers (ARBs) has been a major therapeutic advance in the management of hypertensive patients. This study was designed to compare adverse effects on renal markers in treatment with two commonly used drugs Perindopril and Telmisartan in cases of Hypertension. This was an 'observational' and 'cross-sectional' study.

Methods: This study was conducted in two groups, Group A (Newly diagnosed hypertensive patients) and Group B (Old but poorly controlled hypertensive), each had 100 patients. 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 to response and increased to 8 mg OD and 80 mg OD for Perindopril and Telmisartan respectively to keep mean arterial pressure between 90–115 mmHg. The adjusted dose was kept constant in both groups. Blood urea, serum creatinine and creatinine clearance was estimated initially and then at 4th, 12th and 24th week.

Results: Treatment with Perindopril showed that mean baseline values for blood urea, serum creatinine and creatinine clearance in newly diagnosed and old hypertensive patients were 30.88, 1.37, 64.09 and 33.68, 1.53, 55.98, respectively. After study period these values were 32.24, 1.40, 63.97 and 29.80, 1.46, 59.23 respectively (p value > 0.05). Treatment with telmisartan showed that mean baseline values of blood urea, serum creatinine and creatinine clearance in both group of patients were 30.88, 1.52, 59.32, and 31.72, 1.40, 65.67, respectively. After treatment these values in both groups were 31.92, 1.43, 61.66; and 32.20, 1.46, 61.70, respectively (p value >0.05).

Conclusion: It concluded that both Perindopril and Telmisartan significantly reduces systolic, diastolic and mean arterial pressure without any significant effect on renal function in both newly diagnosed and old hypertensive patients.

Keywords: Perindopril, Telmisartan, Hypertension, Blood urea, Serum creatinine and Creatinine clearance

INTRODUCTION

Systemic arterial hypertension is a condition that affects almost one 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 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 per cent of patients, the cause of hypertension is unknown which is called primary or essential hypertension [5]. The remaining 5-10 per cent 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]. Acute renal failure (particularly in patients with bilateral renal artery stenosis or stenosis of the renal artery of a solitary kidney) is common in all Angiotensin converting enzyme inhibitors [8, 9].

Telmisartan is an ARBs [10], it blocks the action of angiotensin at AT-1 receptor in vascular smooth muscle and adrenal gland causing fall in blood pressure. ARBs can cause hypotension, oliguria, progressive azotemia, or acute renal failure [11].

The study is being undertaken to compare the effects of perindopril and Telmisartan on renal function in treatment of hypertension.

MATERIALS AND 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 Institution 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 was 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 as per previous study [12,13].

Source: Patients attended OPD of general medicine and cardiology and admitted in different unit of department of medicine of IGIMS, Patna.

Inclusion criteria:

Patient selected for 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 month period and prescribed two or more anti-hypertensive medications).

3. Range of blood pressure in study group ≥140/90 and ≤180/110 mm Hg.

Exclusion Criteria

1. Patient with known sensitivity to ACE inhibitor or angiotensin receptor blocker.

2. Pregnant and lactating women.

3. Patient with H/O angioedema.

4. Patient with hepatic impairment.

5. 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-randomised 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 dose was increased to keep mean arterial pressure between 90–115 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 [14].

Following investigations were done to know the renal function of patients during treatment.

1. Blood urea

2. Serum creatinine

3. Creatinine clearance

These investigations were performed initially before starting

treatment and repeated after 4th, 12th and 24th week after starting treatment.

RESULTS

DISCUSSION

Perindopril is an effective antihypertensive agent with an acceptable side effect profile in patients of hypertension [15]. No significant changes were observed in creatinine clearance and it was concluded that perindopril normalizes blood pressure without affecting glycemic control or renal function [16]. Other study it was observed that perindopril showed no significant change in any of metabolic parameters like lipid profile, glucose tolerance, body weight or BMI and the drug was well tolerated and creatinine clearance was unaltered by treatment [17].

The statistical test used for analysis was ANOVA.

In Perindopril group 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 study period these values were 118.72, 119.12 and 81.52, 78.50, respectively (p-value < 0.05). In Telmisartan group 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 study period these values were 118.64, 120.00 and 78.96, 88.16, respectively (p-value < 0.05).

The effect of perindopril on renal function is shown in [Table/Fig-1–4]. This showed that mean baseline values for blood urea, serum creatinine and creatinine clearance in newly diagnosed and old hypertensive patients were 30.88, 1.37, 64.09 and 33.68, 1.53,

55.98, respectively. After study period these values were 32.24,

1.40, 63.97 and 29.80, 1.46, 59.23, respectively. p-value of this study was > 0.05. This failed to show any significant effect on renal function in either newly diagnosed or old hypertensive patients.

A study observed that Telmisartan 40 mg once daily was effective and well tolerated in treatment of mild to moderate hypertension.

[18] The ONTARGET 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 efficacy of Telmisartan and enalapril. It was concluded in the study

	Blood urea (mg/dL)					Serum creatinine (mg/dL)					Creatinine Clearance (mL/min)				
	Mean	±SD	±SEM	*t*-value	*p*-value	Mean	±SD	±SEM	*t*-value	*p*-value	Mean	±SD	±SEM	*t*-value	*p*-value
Initial	30.88	6.49	1.30	-	-	1.37	0.442	0.088	-	-	64.09	20.99	2.97	-	-
4th week	31.72	6.22	1.38	0.58	>0.05	1.32	0.442	0.887	0.17	>0.05	63.88	17.61	2.49	0.052	>0.05
12th week	30.26	7.12	1.29	0.66	>0.05	1.41	0.443	0.089	0.18	>0.05	64.26	18.43	2.60	0.040	>0.05
24th week	32.24	6.82	1.32	0.64	>0.05	1.40	0.443	0.089	0.18	>0.05	63.97	24.27	3.43	0.029	>0

[Table/Fig-1]: Effect of perindopril on renal function in newly diagnosed hypertensive patients.

	Blood urea (mg/dL)					Serum creatinine (mg/dL)					Creatinine Clearance (mL/min)				
	Mean	±SD	±SEM	*t*-value	*p*-value	Mean	±SD	±SEM	*t*-value	*p*-value	Mean	±SD	±SEM	*t*-value	*p*-value
Initial	33.68	6.26	1.25	-	-	1.53	0.443	0.08	-	-	55.98	19.65	2.78	-	-
4th week	29.72	6.16	1.28	3.19	>0.05	1.42	0.444	0.07	0.62	>0.05	60.82	18.38	2.60	1.24	>0.05
12th week	31.82	5.76	1.19	3.26	>0.05	1.43	0.458	0.08	0.58	>0.05	62.83	19.06	2.70	1.76	>0.05
24th week	29.80	5.82	1.16	3.25	>0.05	1.46	0.466	0.09	0.64	>0.05	59.23	20.63	2.92	0.84	>0.05

[Table/Fig-2]: Effect of perindopril on renal function in old hypertensive patients.
p-value of this study is > 0.05. This failed to show any significant effect of Perindopril on renal function in either newly diagnosed or old hypertensive patients

	Blood urea (mg/dL)					Serum creatinine (mg/dL)					Creatinine Clearance (mL/min)				
	Mean	±SD	±SEM	*t*-value	*p*-value	Mean	±SD	±SEM	*t*-value	*p*-value	Mean	±SD	±SEM	*t*-value	*p*-value
Initial	30.88	6.51	1.30	-	-	1.52	0.43	0.082	-	-	59.32	20.87	2.95	-	-
4th week	32.82	6.28	1.29	0.52	>0.05	1.49	0.41	0.080	0.82	>0.05	56.21	16.53	2.34	0.77	>0.05
12th week	30.76	7.05	1.26	0.48	>0.05	1.40	0.39	0.087	0.76	>0.05	60.08	19.85	2.81	0.19	>0.05
24th week	31.92	6.68	1.34	0.54	>0.05	1.43	0.42	0.086	0.73	>0.05	61.66	22.57	3.19	0.58	>0.05

[Table/Fig-3]: Effect of telmisartan on renal function in newly diagnosed hypertensive patients.

	Blood urea (mg/dL)					Serum creatinine (mg/dL)					Creatinine Clearance (mL/min)				
	Mean	±SD	±SEM	*t*-value	*p*-value	Mean	±SD	±SEM	*t*-value	*p*-value	Mean	±SD	±SEM	*t*-value	*p*-value
Initial	31.72	5.69	1.14	-	-	1.40	0.43	0.087	-	-	65.67	24.64	3.49	-	-
4th week	30.82	5.52	1.17	0.31	>0.05	1.39	0.44	0.088	0.52	>0.05	66.67	21.85	3.09	0.22	>0.05
12th week	29.78	5.89	1.19	0.29	>0.05	1.42	0.38	0.086	0.60	>0.05	62.82	21.51	3.04	0.63	>0.05
24th week	32.20	5.79	1.16	0.32	>0.05	1.46	0.40	0.081	0.56	>0.05	61.70	21.79	3.08	0.88	>0.05

[Table/Fig-4]: Effect of telmisartan on renal function in old hypertensive patients.
p-value of this study is > 0.05. This failed to show any significant effect of telmisartan on renal function in either newly diagnosed or old hypertensive patients

that telmisartan is well tolerated and at least as effective as enalapril in treating elderly patients with mild to moderate hypertension [19].

This study showed the effect of telmisartan on renal function in newly diagnosed and old hypertensive patients, respectively. It showed that mean baseline values of blood urea, serum creatinine and creatinine clearance in both groups of patients were 30.88, 1.52, 59.32, and 31.72, 1.40, 65.67, respectively. After treatment these values in both groups were 31.92, 1.43, 61.66; and 32.20, 1.46, 61.70, respectively. P-value of the study was > 0.05. This failed to show any significant effect of telmisartan on renal function in either newly diagnosed or old hypertensive 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 reduction of renal function. Their antihypertensive effects were almost equal and comparable. Study should be done on larger population to substantiate these observations.

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CONFLICT OF INTEREST

We declare that we have no proprietary, financial, professional or other personal interest of any nature or kind in any product, services/ company that could be in conflict with this manuscript entitled “Study of Changes in Renal Function by Perindopril and Telmisartan during Treatment of Systemic Hypertension.”

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