ORIGINAL ARTICLE

Comparative study of efficacy and tolerability of Olmesartan with Ramipril in Type II diabetic and hypertensive Patients

Jaya Babu Nagula [1], Mohd Rasheeduddin [2], Laxman Reddy Nadithe [3], Ravi Shankar Bhairi [4]

1. Tutor, Dept of Pharmacology, Rajiv Gandhi Institute of Medical Sciences (RIMS) Adilabad.
2. 3,4- Senior Residents Dept of Pharmacology, Rajiv Gandhi Institute of Medical Sciences Adilabad.

Abstract

***Background**: Type 2 Diabetes Mellitus is commonly associated with hypertension. The renin-angiotensin-aldosterone system (RAAS) plays a pivotal role in the pathogenesis of insulin resistance and cardiovascular disease in diabetes. Interruption of the RAAS with Angiotensin II type 1, (AT) receptor blockers (ARB) has been shown to prevent or reduce cardiovascular and renal disease progression in diabetic patients with hypertension. With this background we tried to evaluate the efficacy and tolerability of Olmesartan and Ramipiril. **Methods**: Study was conducted on 60 patients who were known diabetics and hypertensive attending the General Medicine clinic of Prathima Institute of medical Sciences Karimnagar. **Results**: The mean difference of 16 in SBP and mean difference of 7.69 in DBP in Ramipril group. Similarly mean difference of 19.8 in SBP and mean difference of 10 in DBP in Olmesartan group. The changes in both groups were statistically significant t-test shows the changes in Olmesartan group was found to be significant. There was mean difference of 4.19 in serum urea, mean difference of 0.05 in serum creatinine and mean difference of 8.21 in albuminuria in Ramipril group. Similarly mean difference of 4.44 in serum urea, mean difference of 0.13 in serum creatinine and mean difference of 24.8 in albuminuria in Olmesartan group. The changes in both groups were statistically significant t-test comparison of the changes in Olmesartan group was found to be significant. **Conclusions**: Olmesartan is a better choice in patients with type 2 Diabetes Mellitus with hypertension in comparison to Ramipril because of Better antihypertensive effect with achievement of target level blood pressure Better glycemic control (both short term and long term). Better improvement of serum creatinine and Urinary Albumin to Creatinine ratio and Good tolerability.*

***Keywords**: Olmesartan, Ramipril, Diabetes Mellitus*

Address for correspondence: Dr Nagula Jaya Babu H.No. 2-5-79, Near Old Bus stand, Post Sircilla District Karimnagar- 505301. Email: jayababu_nagula@yahoo.co.in Mobile: 9885930005.

Received on : 11/01/2016 Revised : 04/02/2016 Accepted : 06/02/2016

Introduction

India leads the world with largest number of diabetes subjects According to the Diabetes Atlas 2006 published by the International Diabetes Federation, the number of people with diabetes in India currently around 40.9 million is expected to rise to 69.9 million by 2025 unless urgent preventive steps are taken. [1] Even though the prevalence of micro vascular complication of diabetes like retinopathy and nephropathy are comparatively lower in Indians, the prevalence of premature coronary artery disease is much higher in Indians compared to other ethnic groups. The most disturbing trend is the shift in age of onset of diabetes to a younger age in the recent years. This could have long lasting adverse effects on nation's health and economy 1 the incidence and prevalence of hypertension among diabetic patients have been documented in various populations and is probably 1.5-2 times higher overall than in non-diabetic people. In western societies, established hypertension is found in 10-30% of patients with IDDM of various durations, and appears to be very closely associated with diabetic nephropathy in IDDM. [2, 3] With this background we tried to evaluate the efficacy and

tolerability of two most commonly used Drugs in Treatment of Hypertension in Diabetic Patients.

Materials & Methods

The present study is a randomized (systemic), open labeled (non-blinded), comparative clinical study between Olmesartan and Ramipril in hypertensive, type II diabetic patients conducted in single center. The study was conducted on 60 patients of hypertension with type II diabetic mellitus attending the Department of General Medicine, Prathima Institute of Medical Sciences, Nagunur, Karimnagar, between the periods of Sep 2012 - Sep 2013. Procedures followed in this study are in accordance with the ethical standard laid down by ICMR's Ethical guidelines for biomedical research on human subjects (2000). The Patients were divided randomly in two groups Olmesartan group (n=30) patients were in this group who received Olmesartan 40mg.tab orally once daily for12 weeks as the treatment for hypertension. Along with oral hypoglycemic agents.(Metformin 500mg tab.) Ramipril group (n= 30) patients were in this group who received Ramipril 5mg.tab orally once daily for 12 weeks as the treatment for hypertension along with oral hypoglycemic agents. (Metformin 500mg tab.) *Inclusion criteria:* Patients with type II diabetes mellitus with hypertension (BP ≥140/90 mmHg) were included in the study. Patients were free from other significant morbidity. Patients of both sex aged 30 years or above. *Exclusion criteria:* Patients who are already on other anti-hypertensive drugs or concurrent medicines (like potassium sparing diuretics, NSAIDs). Pregnant and nursing females. Patients hypersensitive to either group of drugs. Physical examination including, height, weight, BMI, abdominal circumference were assessed. Informed consent was be taken from all the patients who participated in the study after explaining expected advantages and known side effects of Olmesartan / Ramipril and ICMR's Ethical guidelines for biomedical research on humans subjects (2000) were be followed. No medication that could interfere with the clinical evaluations was allowed during the trials. In 12 weeks follow-up, 4 patients discontinued in Ramipril group and in Olmesartan group 5 patients discontinued. So finally, in Ramipril group 26 patients and in Olmesartan group 25 patients completed this trial. Fasting and post-prandial blood sugar: Glucose Oxides – Peroxidase (GOD-POD) method. Glycosylated Hb (HbA1c%): Chromatographic spectrphotometric ion exchange. Serum urea: Enzymatic method with salicylate. Serum creatinine: Jaffe method. Cholesterol was estimated by "CHOD-PAP": Enzymatic photometric test. [4] Triglycerides were estimated Colorimetric enzymatic test using glycerol-3-phosphate oxidase(GPO). [5] HDL Cholesterol was estimated by Phopho tungstate method. [6]

Results

The baseline demographic data and clinical characteristics of all 60 patients participated in this study have been compared in the Table 1 and P values suggests that there is no statistically significant difference in between the study groups in the parameters studied in the first visit.

To assess the antihypertensive effect of both the drugs, blood pressure in sitting position was measured at both the visits and was compared statistically. The results have been shown in the Table 4 and also presented in bar diagram.

There was a mean difference of 16 in systolic blood pressure and mean difference of 7.69 in diastolic blood pressure in Ramipril group. Similarly mean difference of 19.8 in systolic blood pressure and mean difference of 10 in diastolic blood pressures in Olmesartan group. The changes in both groups were statistically significant. But when the mean difference of two groups were compared by unpaired t-test, the changes in Olmesartan group were found significant.

***Assessment of renal profile*:**

There was mean difference of 4.19 in serum urea, mean difference of 0.05 in serum creatinine and mean difference of 8.21 in albuminuria in Ramipril group. Similarly mean difference of 4.44 in serum urea, mean difference of 0.13 in serum creatinine and mean difference of 24.8 in albuminuria in Olmesartan group. The changes in both groups were statistically significant. But when the mean differences of two groups were compared by unpaired t-test, the changes in Olmesartan group were found to be significant.

Table- 1: Baseline demographic data and clinical characteristics of the 60 patients of type 2 diabetes mellitus with hypertension participated in the study in the first visit

Characteristics	Ramipril group	Olmesartan group	P value
Number of the patients recruited	30	30	
Number of the patients at follow up	26	25	
Female patients (%)	46.6	43.4	
Age (years)	53.5 ± 9.26	48.8 ± 9.9	0.06
Duration of diabetes (years)	7.73 ± 3.78	6.97 ± 3.3	0.409
Height(meters)	1.5840±.09633	1.5940± .09141	0.68
Weight(kg)	67.33± 10.077	67.67± 13.476	0.91
BMI (Kg/m2)	27.05±4.23	26.32±5.24	0.56
Waist circumference (Inch.) ABC	38.25±5.30	36.75±3.91	0.21
Systolic blood pressure (mm Hg.)	154.07±8.31	151.53±9.51	0.27
Diastolic blood pressure (mm Hg)	94.47±4.59	92.73±3.38	0.10
HbA1c%	7.50±1.73	7.29±1.59	0.61
Fasting blood sugar (mg/dl)	164.40±38.0	159.73±35.1	0.62
Post-prandial blood sugar(mg/dl)	246.6±53.4	243.6±47.8	0.82
Triglyceride (mg/dl)	146.06±63.933	157.07± 71.430	0.53
Total cholesterol (mg/dl)	178.03±37.0	180.29±32.9	0.80
LDL cholesterol (mg/dl)	111.15±31.9	115.41±32.2	0.60
HDL cholesterol (mg/dl)	41.10± 7.976	41.17± 5.484	0.97
VLDL (mg/dl)	25.00± 13.409	23.73± 12.446	0.70
Serum urea (mg/dl)	55.30± 12.393	58.60± 13.174	0.32
Serum creatinine (mg/dl)	1.307± .5199	1.547± .5224	0.08
Number of patient with micro albuminuria (%)	144.27±76.792	149.17± 89.678	0.82

Data are in Mean ± SD, LDL- Low density lipoprotein, VLDL- Very low density lipoprotein, HDL- High density lipoprotein

Table 2: Changes in systolic and diastolic blood pressure in study groups.

Parameters	Ramipril group				Olmesartan group			
	1ST visit	2nd visit	Mean	P value	1ST visit	2nd visit	Mean	P value
SBP(mm of Hg)	153.69 ±8.01	137.69 ±6.63	16	0.003$	150.8 ±10.24	131.04 ±10.2	19.8	<0.001$
DBP(mm of Hg)	94.15 ±4.07	86.46 ±4.53	7.69	0.004$	93.04 ±3.5	83.04 ±3.5	10	0.027$

Data are in Mean ± SD, $ Paired t-test. *unpaired t-test

Table 3: Changes in renal parameters in study groups

Parameters	Ramipril group				Olmesartan group			
	1st visit	2nd visit	Mean	P value	1st visit	2nd visit	Mean	P value
Serum Urea (mg/dl)	56.23 ±11.99	52.04 ±8.5	4.19	<0.001$	58.84 ±12.39	54.4 ±8	4.44	<0.001$
Serum Creatinine (mg/dl)	1.32 ±0.51	1.27 ±0.46	0.05	<0.001$	1.54 ±0.49	1.41 ±0.44	0.13	<0.001$
Albuminuria	141.31 ±81.204	133.12 ±70.93	8.21	0.004$	151.16 ±83.85	126.36 ±74.62	24.8	<0.001$

Data are in Mean ± SD $ Paired T-test, * unpaired t-test.

Table: 4: Side effects complained by the patients in study groups.

SIDE EFFECTS	RAMIPRIL GROUP	OLMESARTAN GROUP
Nausea/vomiting	1	1
Rash	1	1
Cough	1	0
Hypotension	1	1
Total	4	3

***Assessment of Safety*:**
Both the drugs were well tolerated without any alarming side effects. In Ramipril group one patient complains of nausea, one patient had mild skin rash, one patient suffered from cough and one patient suffered from hypotension. One patient who was on Olmesartan complains nausea, one had hypotension and another one patient suffered from skin rash in initial few days.

Discussion

The baseline demographic data confirmed the homogeneity of the groups and showed that 36.7% patients were in the age group of 41-50 years, and 55% were male. The patients were suffering from diabetes for an average duration of 7 years. More than three fourth of the patients were found to be overweight and diagnosed as cases of metabolic syndrome. In a similar study by Stefano Omboni et al [7], comparing efficacy and safety of the Angiotensin II Receptor blocker Olmesartan Medoxomil and the Angiotensin Converting Enzyme inhibitor Ramipril, in elderly patients with essential hypertension. They concluded that Olmesartan provides more effective BP control than Ramipril in elderly hypertensive patients with and without metabolic syndrome. In a similar study by Jean MM et al; to compare the efficacy and safety of Olmesartan with Ramipril in elderly patients with essential arterial hypertension they found that Olmesartan provided an effective, prolonged and well tolerated blood pressure control with significant normalization as compared with Ramipril group [8]. It is in agreement with our findings where we found Olmesartan had better blood pressure control as compared to Ramipril group. The ESPORT study by Malacco et al; comparing efficacy and safety of Olmesartan and Ramipril in elderly patients with mild to moderate essential hypertension found that Olmesartan provided effective and prolonged well tolerated BP control and they concluded that Olmesartan was a useful first line drug in treatment of hypertension in this age group [9].
One study by Ettore Malacco et al; comparing the renal function status in elderly patients with mild to moderate hypertension with use of Olmesartan and Ramipril found that borderline BP reductions were superior with Olmesartan then with Ramipril. However no significant differences in Kidney function were noted [10]. In our Study we found slight improvement in Renal profile of patients with Olmesartan then compared with Ramipril group were noted [11]. The Probable mechanism by which Olmesartan confers better control of BP can be explained by the fact that Olmesartan is a potent blocker of AT1 receptors. This result in complete inhibition of AT1 activation because response to Angiotensin II generated via alternate pathways and consequent AT1 activation which remain intact with ACE inhibitior (Ramipril) are completely blocked. [12]
In another study by Omboni S et al; comparing the efficacy of Olmesartan and Ramipril found the efficacy of olmesartan was not negatively affected by age, sex, hypertension, diabetes or other concominant clinical conditions or cardiovascular risk factors [18]. Olmesartan provided better blood pressure control than Ramipril which was in complete agreement with the present study.

Conclusion

From the present clinical study it can be concluded that Olmesartan is a better choice in patients with type 2 Diabetes Mellitus with hypertension in comparison to Ramipril because of better antihypertensive effect with achievement of target level blood pressure. Better glycemic control (both short term and long term) and improvement of serum creatinine and Urinary Albumin to Creatinine ratio. Good tolerability.

Conflict of Interest: *None declared*
Source of Support: *Nil*
Ethical Permission: *Obtained*

References

1. V. Mohan, S. Sandeep, R. Deepa, B. Shah, and C. Varghese. Epidemiology of type 2 diabetes: Indian scenario. Indian J Med Res 2007; 125: 217-230.
2. Ismail N, Becker B, Strzelczyk P, Ritz E: Renal disease and hypertension in non-insulin-dependent diabetes mellitus. Kidney Int 1999; 55:1-28.
3. Bojestig M, Arnqvist H, Hermansson G, Karlberg B, Ludvigsson J: Declining incidence of nephropathy in insulin-dependent diabetes mellitus. N Engl J Med 1994; 330:15-18.
4. Allain CC, Poon LS, Chan CSG, Richmond W, Fu Pc. Enzymatic determination of Total Serum Cholesterol. Clin Chem 1978;20:470-475.
5. MW McGowan, JD Artiss, DR Strandberg, B Zak. A peroxidase coupled method for coloriemetric determination of serum triglycerides. Clin Chem 1983;29(3):538-542.
6. Assmann G, Schriewer H, Schintz G, et al; Qualification of high density lipoprotein cholesterol by precipitation with phosphotungstic acid/MgCl2. Clin Chem 1983;29:2026-2030.
7. Stefano Omboni, Ettore Malacco, Jean-Michel Mallion, Massimo Volpe. Antihypertensive Efficacy and Safety of Olmesartan Medoxomil and Ramipril in Elderly mild to moderate essential Hypertensive Patients with or without Metabolic Syndrome. Drugs and aging 2102; 29(12): 981-992.
8. Jean MM, Stefano O, John B, Walter VM, Krzysztof N, Peter-Klaus P, et al. Antihypertensive efficacy and safety of olmesartan and ramipril in elderly patients with mild to moderate systolic and diastolic essential hypertension. Blood Pressure 2011; 20(1):3-11.
9. Malacco, Ettore, Omboni, Stefano, Volpe, Massimo, Auteri, Alberto, Zanchetti, Alberto, Antihypertensive efficacy and safety of olmesartan medoxomil and ramipril in elderly patients with mild to moderate essential hypertension: the ESPORT study. J of Hypertension 2010; 28(11): 2342-50.
10. Ettore M, Stefano O, Jean-MM, Massimo V, the ESPORT Study Group. Antihypertensive Efficacy of Olmesartan Medoxomil and Ramipril in Elderly Patients with Mild to Moderate Hypertension Grouped According to Renal Function Status. High Blood pressure and Cardiovascular Prevention 2012; 19(4): 213-222.
11. KD Tripathi. Drugs affecting Renin Angiotensin System and Plasma Kinins. Essentials of Medical Pharmacology 7th Edn Jaypee Brothers Medical Publishers 2014; 496-508.
12. Omboni S, Malacco E, Mallion JM, Volpe M. Olmesartan vs ramipril in the treatment of hypertension and associated clinical conditions in the elderly: a reanalysis of two large double-blind, randomized studies at the light of the most recent blood pressure targets recommended by guidelines. Clinc Interv Aging 2015; 10:1575-86.