Original Article

Comparison of Efficacy of Lisinopril and Losartan for Reducing Microalbuminuria Levels in Patients with Type-2 Diabetes Mellitus

Roney Javed, Suresh Kumar, Naresh Kumar Khurana, Anil Kumar, Asma Hameed and Naeem Khan Durrani

ABSTRACT

Objective: To compare the efficacy of losartan and lisinopril for reduction of microalbuminuria in patients with type-2 diabetes mellitus.

Study Design: Randomized Control Trial study

Place and Duration of Study: This study was conducted at the Department of Medicine, Bolan Medical Complex Hospital, Quetta, Pakistan from July 2019 to January 2020.

Materials and Methods: A total of 110 with diagnosed type II diabetes mellitus and albumin to creatinine ratio 30–300 mcg/mg creatinine in the 1st early morning urine, age 18-75 of both genders were included. Patients with hypersensitivity to ACE inhibitors or Angiotensin Receptor Blocker, CRF, pregnancy and uncontrolled hypertension were excluded. All the patients were randomly divided into two groups by the lottery method. Group A was treated with 100 mg of Losartan potassium for 12 weeks while Group B patients were given 5 mg of Lisinopril for 12 weeks.

Results: The mean age of patients in group A was 39.60 ± 10.12 years and in group B was 41.0 ± 8.05 years. Majority of the patients 56 (50.91%) were between 18 to 45 years of age. Out of 110 patients, 47 (42.78%) were males and 63 (57.27%) were females with male to female ratio of 1:1.3. Efficacy of Group A (losartan group) was seen in 48 (87.27%) patients while in Group B (lisinopril group) was seen in 37 (67.27%) patients (p-value = 0.012)

Conclusion: This study concluded that efficacy of losartan is higher than lisinopril for reduction of microalbuminuria in patients with type-2 diabetes mellitus.

Key Words: type II diabetes, microalbuminuria, losartan

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INTRODUCTION

Diabetes mellitus (DM) is a growing public health concern with multiple complications, affecting more than 415 million individuals around the globe and expected to reach 642 million individuals by end of 2040 [1-2]. Past examinations detailed the predominance of DM in Pakistan going from 7.6% to 11% and assessed to reach 15% of absolute populace by 2030 [3]. Different miniature and full-scale vascular inconveniences are related with sickness movement particularly diabetic nephropathy (DN) that outcomes from the durable impacts of DM on the glomerular microvasculature of the kidney [4]. Around 30-40% of type II diabetic patients foster DN notwithstanding severe blood glucose and additionally circulatory strain control [5]. The principal markers of DN are constant albuminuria, hypertension, and reformist renal harm[6,7]. Angiotensin changing over compound (ACE) inhibitors e.g., lisinopril seriously block the renin angiotensin framework, and decrease the glomerular slender strain and turn away improvement of microalbuminuria to plain proteinuria. Some different examinations likewise detailed a practically identical beneficial effect of angiotensin II receptor blockers (ARB) e.g., losartan in relapse of microalbuminuria to unmistakable proteinuria [8]. In a new report, Sandhu GA et al thought about the adequacy of ACE inhibitor (Lisinopril) and ARB (Losartan Potassium) as far as decrease in microalbuminuria in Type II DM patients. Viability of medication was seen in 86.7% patients (n=26) in Losartan potassium bunch while 66.7% patients (n=20) in lisinopril bunch [9].

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DN builds the danger for sudden passing, cardiovascular infection, and other serious diseases that outcome in continuous hospitalizations and expanded health-care use. Decrease in microalbuminuria is a significant prognostic factor in the administration of DN [10]. Another metanalysis reasoned that ACEIs and ARBs are likewise compelling for treating microalbuminuria[11]. Thus, in view of as of late distributed writing, both are regularly utilized in our setting for treating raised microalbuminuria, however as far as I could possibly know, no review has done that thought about the viability of these medications for treatment of microalbuminuria in Type II DM patients of our populace. The reasoning of this review is to analyze the impacts of ACE inhibitors and ARBs on microalbuminuria in Type II DM patients. The review results will assist with deciding the better treatment choice for treating microalbuminuria in patients with DN and will be utilized as medication of decision for the treatment of these patients in future.

Better treatment option will ultimately help to reduce morbidity and mortality associated with diabetic nephropathy.

MATERIALS AND METHODS

Study design: This Randomized Control Trial was conducted in Department of Medicine, Bolan Medical Complex Hospital, Quetta during 20th July 2019 to 21st January 2020.

Sample size: The sample size was calculated using the WHO Sample Size Calculator:

Sample Size: Eighty patients n=110 (55 patients in each group).

Sample technique: Non-probability, consecutive sampling.

Sample selection:

Inclusion Criteria:

a. Patients with diagnosed type II diabetes mellitus and albumin to creatinine ratio 30–300 mcg/mg creatinine in the 1st early morning urine as described in operational definition
b. Age between 18 to 75 years.
c. Both Genders

Exclusion Criteria:

a. Patients with chronic heart failure
b. Pregnant and lactating female
c. Patients with known hypersensitivity to ACE inhibitors or Angiotensin Receptor Blocker
d. Patients with uncontrolled hypertension.
e. Patients who are being treated with any investigational drug within the last 30 days.

Data collection procedure: Study was started after taking prior approval and permission from the hospital ethical committee. Blood sample of all the patients diagnosed with DM type-2 presented to the hospital were taken and sent to laboratory for performing fasting blood glucose and 1st morning Urine sample was taken and analyzed for albumin to creatinine ratio of these patients. Patients with type II DM and microalbuminuria as defined in operational definition and fulfilling the other inclusion criteria were enrolled for study. By taking informed written consent from all the patient, the thorough physical examination was performed after taking detailed clinical history. All the patients were randomly divided into two groups by the lottery method. Group A was treated with 100 mg of Losartan potassium for 12 weeks while Group B patients were given 5 mg of Lisinopril for 12 weeks. After 12 weeks therapy the efficacy of the drug was determined in both groups as per our operational definition. For this purpose, albumin to creatinine ratio was determined from the hospital laboratory by analysis of 1st early morning urine after 12 weeks of treatment. All the data collection was performed by the trainee researcher himself to main data quality and compliance and study results were recorded in the prescribed proforma attached as annexure I.

Data analysis procedure: Data was entered and analyzed on SPSS version 20.0. Frequency and percentages were computed for qualitative variable like gender and efficacy among two groups. Quantitative variables like Age, fasting blood glucose level, height, weight, BMI & baseline albumin to creatinine ratio (microalbuminuria) and at 12-week therapy were presented by mean and standard deviation. Chi square test was used to compare the efficacy of both groups. P value ≤ 0.05 was considered significant.

RESULTS

The age range of patients in this research was from 18-75 years. The mean age of patients was 40.35 ± 8.65 years. In group A the mean age of patients was 39.60 ± 10.12 years and in group B was 41.0 ± 8.05 years. As shown in Table I, most of the patients were between 18 to 45 years of age and number of patients were 56 (50.91%).

There were 110 total patients and out of those 110 patients, the number of males patients were 47 (42.78%) and number of females patients were 63 (57.27%), the male to female ratio were 1:1.3. As shown in Table 2, the mean BMI was 29.12 ± 3.41 kg/m^2. Mean height was 165.86 ± 14.76 cm. Mean weight was 75.63 ± 8.35 cm. Most of the patients 64 (58.12%) were with the BMI of ≤ 30 kg/m^2.

Efficacy of Group A (losartan group) was seen in 48 (87.27%) patients while in Group B (lisinopril group) was seen in 37 (67.27%) patients (p-value = 0.012).

Stratification of efficacy with respect to age groups is shown in Table 3. The P-value of patients with the age group of 28-45 years was 0.350 and 46-75 years was 0.021. Results showed that the age group of 28-45 years showed more positive results compared to the other age group in both group A and Group B. The number of patients in both group A and B was 55.

Table No.1: Age distribution for both groups (n=110)

Age (years)	Group A (n=55)		Group B (n=55)		Total (n=110)	
	No. of patients	%age	No. of patients	%age	No. of patients	%age
18-45	37	67.27	39	70.91	56	50.91
45-75	18	32.78	16	29.09	34	49.09
Mean ± SD	39.60 ± 10.12		41.0 ± 8.05		40.35 ± 8.65	

Table No.2: Percentage of patients according to BMI (n=110)

BMI	Group A (n=55)		Group B (n=55)		Total (n=110)	
	No. of patients	%age	No. of patients	%age	No. of patients	%age
≤30 kg/m^2	32	58.18	32	58.18	64	58.12
>30 kg/m^2	23	41.82	23	41.82	46	41.82
Mean ± SD	29.15 ± 3.42		29.05 ± 3.34		29.12 ± 3.41	

Table No.3: Stratification of efficacy with respect to age groups

Age of patients (years)	Group A (n=55)		Group B (n=55)		P-value
	Efficacy		Efficacy		
	yes	no	yes	no	
28-45	31	06	27	12	0.350
46-75	17	01	10	06	0.021

Table No.4: Stratification of efficacy with respect to gender

Gender	Group A (n=55)		Group B (n=55)		P-value
	Efficacy		Efficacy		
	yes	no	yes	no	
Male	22	02	15	08	0.027
Female	26	05	22	10	0.159

Table No.5: Stratification of efficacy with respect to BMI

BMI	Group A (n=55)		Group B (n=55)		P-value
	Efficacy		Efficacy		
	yes	no	yes	no	
≤30 kg/m^2	29	03	23	09	0.055
>30 kg/m^2	19	04	13	09	0.082

Stratification of efficacy with respect to age groups and gender is shown in Table 4. The P-value of the gender male was 0.027 and female was 0.159. Female showed more positive results than male in both Group A and group B. The number of patients in both groups were 55.

In Table 5 the stratification of efficacy showed with respect to BMI. The P-value of BMI ≤30 kg/m^2 was 0.055 and the number of patients in group A was 55 and group B was also 55. The number of yes efficacies in those patients in group A was 29 and in group B, it was 23 and the negative numbers were 3 and 9, respectively. The P-value of BMI >30 kg/m^2 was 0.082. The number of yes efficacies in those patients in group A was 19 and in group B, it was 13 and the negative numbers were 4 and 9, respectively.

DISCUSSION

The risk for cardiovascular and renal disease increases in type II diabetes after the growth of microalbuminuria[12-14]. In type II diabetes the prevalence rate of renal disease (end-stage) has increased in many areas globally [15,16]. According to recent studies, for the protection of renal and possibly cardio protection, the main treatment goal is the regularization and reduction of proteinuria [17]. In the diabetic animal model, the inhibition of (RAS) renin-angiotensin system (by ACE inhibitors or (AIIAs) angiotensin II antagonists) prevents the growth of proteinuria or lowers the level of proteinuria which results in less damage of renal structure [18,19]. ACE inhibitor therapy reduces the albumin excretion rate (UAER) in type II diabetic patients with microalbuminuria, and as determined by serum creatinine, it also prevents the growth and development of renal disease [20]. AIIAs selectively block the AT1 receptor which reduces microalbuminuria in these patients to the same level as ACE inhibition [21].

I have conducted this study to compare the efficacy of losartan and lisinopril for reduction of microalbuminuria in patients with type-2 diabetes mellitus. Age range in this study was from 18-75 years with mean age of 40.35 ± 8.65 years. In group A the mean age of patients was 39.60 ± 10.12 years and in group B was 41.0 ± 8.05 years. Majority of the patients 56 (50.91%) were between 18 to 45 years of age. Out of

110 patients, 47 (42.78%) were males and 63 (57.27%) were females, with male to female ratio of 1:1.3. Efficacy of Group A (losartan group) was seen in 48 (87.27%) patients while in Group B (lisinopril group) was seen in 37 (67.27%) patients (p-value = 0.012). In a recent study, Sandhu GA et al compared the efficacy of ACE inhibitor (Lisinopril) and ARB (Losartan Potassium) in terms of reduction in microalbuminuria in Type II DM patients. Their study results showed that mean microalbuminuria levels (mcg/ mg) at 12 weeks of study was reduced from 193±67.5 to 36.33±54.68 in Losartan potassium group and from 209.5±72.0 to 72±83.42 in lisinopril group. Efficacy of drug was observed in 86.7% patients (n=26) in Losartan potassium group while 66.7% patients (n=20) in lisinopril group [(9)].

In patients with type II diabetes, the effect of Reno protective on ARB and ACE inhibitors were studied and, in a study, done by Barnett AH, 250 individuals with type II diabetes and initial stage of nephropathy were casually assigned to receive either the ARB telmisartan, in 120 patients (80 mg/d) or the ACE inhibitor enalapril, in 130 patients (20 mg/d). The main endpoint was the difference in the (GFR) Glomerular filtration rate amongst the standard value and the last obtainable value throughout the five (5) years therapy period. GFR reduced after five (5) years with telmisartan by 17.9 ml per minute, per 1.73 m2 of surface region of body and with enalapril by 14.9 ml per minute, per 1.73 m2, with a therapy difference of 3.0 ml per min, per 1.73 m2. In type II diabetic patients this difference was not sufficient (based on predefined criteria) to conclude that telmisartan is better than enalapril in offering long term renoprotection. For decrease in BP in such patients, combination of lisinopril and candesartan was more effective than monotherapy and the similar trend was evident for the decrease in rate of urinary albumin excretion [(22)].

CONCLUSION

This study concluded that efficacy of losartan is higher than lisinopril for reduction of microalbuminuria in patients with type-2 diabetes mellitus. Majority of the patients 56 (50.91%) were between 18 to 45 years of age. Out of 110 patients, 47 (42.78%) were males and 63 (57.27%) were females.

Author's Contribution:

Concept & Design of Study:	Roney Javed
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Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Akhtar S, Khan Z, Rafiq M, Khan A. Prevalence of type II diabetes in district Dir Lower in Pakistan. Pak J Med Sci 2016;32:622-5.
2. Meo SA, Zia I, Bukhari IA, Arain SA. Type II diabetes mellitus in Pakistan: current prevalence and future forecast. J Pak Med Assoc 2016; 66:1637-42.
3. Hussain A, Ali I. Diabetes mellitus in Pakistan: A major public health concern. Arch Pharma Pract 2016;7:30-2.
4. Nazar CMJ. Diabetic nephropathy; principles of diagnosis and treatment of diabetic kidney disease. J Nephropharmacol 2014;3:15-20.
5. Tomino Y, Gohda T. The prevalence and management of diabetic nephropathy in Asia. Kidney Dis 2015;1:52-60.
6. Ren F, Tang L, Cai Y, Yuan X, Huang W, Luo L, et al. Meta-analysis: the efficacy and safety of combined treatment with ARB and ACEI on diabetic nephropathy. Renal Failure 2015;37: 548-61.
7. Fiseha T. Urinary biomarkers for early diabetic nephropathy in type II diabetic patients. Bio Mark Res 2015; 3:16-8.
8. Sudhakar A, Pasula S, Simpson GB. Efficacy of drugs in controlling microalbuminuria of diabetic nephropathy. Int J Basic Clin Pharmocol 2014; 3:350-3.
9. Sandhu GA, Tahir GA, Ahmad Z, Anjum AM. Microalbuminuria; comparison of losartan potassium and lisinopril in treatment of patients with type ii diabetes mellitus. Profess Med J 2017; 24:221-7.
10. Huang R, Feng Y, Wang Y, Qin X, Melgiri ND, Sun Y, Li XS. Comparative efficacy and safety of antihypertensive agents for adult diabetic patients with macroalbuminuric kidney disease: a network meta-analysis. PLoS One 2017;12: e0168582.
11. Xu R, Sun S, Huo Y. Effects of ACEIs versus ARBs on proteinuria or albuminuria in primary hypertension: a meta-analysis of randomized trials. Medicine (Baltimore) 2015;94(39): e1560.
12. Mogensen C. Microalbuminuria predicts clinical proteinuria and early mortality in maturity onset diabetes. N Engl J Med 1984;310:356–360.
13. Dinneen SF, Gerstein HC. The association of microalbuminuria and mortality in non-insulin-dependent diabetes mellitus: a systematic overview of the literature. Arch Intern Med 1997;157:1413–1418.
14. Mattock MB, Barnes DJ, Viberti GC, et al. Microalbuminuria and coronary heart disease in non-insulin-dependent diabetes: an incidence

study. Diabetes 1998;47:1786–1792.
15. USRDS Annual Data Report Chapter 2. Incidence and prevalence of ESRD. Am J Kidney Dis 1999;34:S40–S50.
16. Pugh JA, Medina RA, Cornell JC, et al. NIDDM is the major cause of diabetic end-stage renal disease: more evidence for a tri-ethnic community. Diabetes 1995;44:1375–1380.
17. Ruggenenti P, Schieppati A, Remuzzi G. Progression, remission, regression of chronic renal disease. Lancet 2001;357:1601–1608.
18. Anderson S, Rennke HG, Brenner BM. Therapeutic advantage of converting enzyme inhibitors in arresting progressive renal disease associated with systemic hypertension in the rat. J Clin Invest 1986;77:1993–2000.
19. Remuzzi A, Perico N, Amuchastegui CS, et al. Short and long-term effect of angiotensin II receptor blockade in rats with experimental diabetes. J Am Soc Nephrol 1993;4:40–49.
20. Ravid M, Savin H, Jutrin I, et al. Long-term stabilizing effect of angiotensin-converting enzyme inhibition on plasma creatinine and on proteinuria in normotensive type II diabetic patients. Ann Int Med 1993;118:577–581.
21. Muirhead N, Feagan BF, Mahon J. The effects of valsartan and captopril on reducing microalbuminuria in patients with type II diabetes mellitus: a placebo- controlled trial. Curr Therapeutic Res 2000;60:650–660.
22. Barnett AH. Diabetics Exposed to Telmisartan and Enalapril Study Group. Angiotensin-receptor blockade versus converting-enzyme inhibition in type II diabetes and nephropathy. N Engl J Med 2004;351:1952-61.