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Effect of Telmisartan and Losartan on Glomerular Filtration Rate (GFR) in Patients with Diabetic Nephropathy

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ABSTRACT

Introduction*: Proteinuric kidney disease is a common consequence of diabetes which is the leading cause of kidney failure and shortens life expectancy. Telmisartan and losartan are the two commonly used drugs in lowering proteinuria and increasing glomerular filtration rate (GFR)in diabetic nephropathy patients. The aim of this study was to compare the effects of telmisartan and losartan in increasing GFR in diabetic nephropathy patients.* ***Methods:*** *This randomized controlled trial (RCT)was conducted at the Department of pharmacology and therapeutics in collaboration with Rajshahi Diabetic Association General Hospital, Rajshahi, from January, 2021 to December, 2021. Total 100 patients suffering from diabetic nephropathy with type 2 diabetes mellitus were enrolled and randomly divided into two groups. Patients in group A (control, losartan group) were given losartan one tablet containing 50 mg once daily for 12 weeks and patients in group B (experimental, telmisartan group) were given telmisartan one tablet 40 mg once daily for same duration. Data collection was carried out by the investigator himself and data analysis was done by SPSS software, version-24.* ***Results:*** *The mean ages of the patients in the losartan and telmisartan group were 64.2±5.70 years and65.9±4.95 years, respectively and male was the predominant gender in both groups (68% in group A and 62% in group B).There was no significant difference in the blood pressure and estimated glomerular filtration rate (eGFR) at the baseline between losartan and telmisartan administered patients (p >0.05). In telmisartan group, the eGFR was significantly (p-0.022) increased from baseline to 12 weeks treatment. There was no significant different of eGFR between the telmisartan and losartan groups after 12 weeks of treatment (p-0.183).* ***Conclusion:*** *Telmisartan is better in increasing eGFR than losartan among diabetic nephropathy patients.*

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INTRODUCTION

Diabetic patients experience a persistent decrease of kidney function, which is referred to as diabetic nephropathy or diabetic kidney disease. It is one of the main causes of end-stage renal illness and chronic kidney disease (CKD) worldwide, affecting over 50% of diabetes individuals.[1]Diabetes is one of the most common non communicable disease globally and is considered epidemic in many developed and industrialized countries.

Complications of diabetes include peripheral and coronary vascular disease, stroke, neuropathy, blindness and kidney failure that cause disability and reduced life expectancy.[2] Diabetic nephropathy, or chronic kidney disease, is one of the most dangerous side effects of diabetes. The term "diabetic nephropathy" implies the presence of a characteristic pattern of glomerular disease and describes a clinical condition marked by persistent albuminuria and a progressive deterioration in renal function.[1] The rennin-angiotensin aldosteron system plays a critical role in diabetic nephropathy because it is triggered by hyperglycemia and glycation end products which in turn cause the production of angiotensin II.[3] The onset and progression of diabetic nephropathy are facilitated by a number of risk factors, such as obesity, high blood glucose, dyslipidemia, raised blood pressure and others. The majority of risk factors are changeable. As a result, it is crucial to provide them with special care in order to stop and slow the deterioration of their renal functions.[4]

Lowering blood pressure and proteinuria by more than 30% is associated with reduced progression of renal failure in diabetic nephropathy.[3] for the majority of diabetic patients with hypertension and diabetic nephropathy, highly selective angiotensin II type 1 receptor blockers (ARBs) are advised as first line therapy because they not only lower blood pressure but also reduce proteinuria. Telmisartan stands out among ARBs due to its strong affinity for the angiotensin II type 1 receptor, prolonged receptor binding duration, high lipophilicity and extended plasma half-life.[5] GFR is the best indicator of total renal function and should be assessed in diabetic individuals with micro and macroalbuminuria. GFR levels in microalbuminuric patients may be steady, however a small percentage of patients have had a sharp drop in GFR. Without treatment, the GFR of type 1 macroalbuminuric patients decreases about 1.2 ml/min/ month. GFR decline varied in persons with type 2 diabetes. According to Gall et al.[6] the mean drop was ~0.5 ml/min/month, while some patients may have long-term stability in their GFR. Patients with DM and CKD frequently have hypertension. Patients with a more rapid GFR decline usually have more advanced diabetic glomerulopathy and worse metabolic control. So, increasing GFR is a prime concern in patients of diabetic nephropathy. Senapaty et al.[7] observed, telmisartan has stronger protective advantages against kidney impairment due to diabetes and hypertension by increasing GFR. The Joint National Committee on Prevention, Detection, Evaluation and Treatment of high blood pressure suggested that, patients with diabetic nephropathy should have their blood pressure below 130/80 mmHg.[8,9] According to certain theories, telmisartan reduces proteinuria in diabetic nephropathy patients more effectively than losartan and therefore eGFR increases.

The aim of this study was to compare the effects of telmisartan and losartan on eGFR in diabetic nephropathy patients.

METHODS

This randomized controlled trial was conducted at the Department of pharmacology and therapeutics in collaboration with Rajshahi Diabetic Association General Hospital, Rajshahi, from January, 2021 to December, 2021. Before commencement of the study, ethical clearance was obtained from the ethical review committee (ERC Number: Ref-RMC/IRB/2021/16) of Rajshahi Medical College, Rajshahi. All diabetic nephropathy patients with type 2 diabetes mellitus and hypertension were approached for this trial. Due to time and resource constraint, total 100 patients suffering from diabetic nephropathy with type 2 diabetes mellitus were enrolled by systematic random sampling and allocation of drugs were done by simple lottery

methods in every two respondents. Inclusion criteria were type 2 diabetes mellitus with total HbA1c ≤10%, blood pressure: Systolic 140-160 mmHg and diastolic 90-100 mmHg, estimated Glomerular filtration rate not less than 50 ml/min/1.73m^2 and spot urinary albumin creatinine ratio 30-300 mg/g creatinine. Exclusion criteria were pregnant women, non diabetic renal disease, congestive heart failure, stroke, hepatic dysfunction and electrolyte imbalance and history of long term immunosuppressive therapy. Patients in group A (control) were given loasrtan 50 mg once daily for 12 weeks and patients in group B (experimental) were given telmisartan 40 mg once daily for same duration. Anti-diabetic drug in each group was given according to condition of patient. Insulin, Repaglinide, Nateglinide, Dipeptidyl peptidase 4 (DPP-4) inhibitor (Linagliptin) were used and Metformin had not been used eGFR below 45 ml/min/1.73 m^{2}and Sulfonylureas (except Glipizide) had not been used because one or more of their metabolites may accumulate resulting in increased risk of hypoglycemia. Blood pressure (systolic and diastolic blood pressure) and eGFR were measured at the commencement and also after 12 weeks of treatment to compare the renoprotective effect of telmisartan and losartan in increasing eGFR. All relevant information from history, clinical findings and investigations were recorded in the separated case record form. Data analysis was done by SPSS software, version-24. Frequency and percentage were used to express categorical variables while mean and standard deviation were used to express continuous variables. To determine the difference between continuous variables, independent sample t test and paired t test were done. For all statistical tests, p-value <0.05 was considered as statistically significant.

RESULTS

The mean ages of the patients in the losartan and telmisartan group were 64.2±5.70 years and 65.9±4.95 years, respectively. In both groups male patients were higher than female. Blood pressure and eGFR were almost similar in control and experimental group (Table I).

Table I: Comparison of baseline variables between the two groups.

Variables	Group		*p* value
	Group A (control, Losartan, n-50)	Group B (experimental, Telmisartan, n-50)	
Mean age (Years)	64.2±5.70 years	65.9±4.95 years	0.17#
Sex			
Male	34 (68%)	31 (62%)	0.67*
Female	16 (32%)	19 (38%)	
Total	**50 (100.00%)**	**50 (100.00%)**	
Baseline Blood Pressure			
SBP (mmHg)	144±4.44	143±4.57	0.297#
DBP (mmHg)	96±15.9	98±21.6	0.489#
eGFR (ml/min/1.73 m^2)	58.7±5.14	57.9±5.21	0.925#

*Chi-squared Test (χ^2) was done to analyze the data #Data were analyzed using Unpaired t-Test and presented as mean ± SD.

After 12 weeks of treatment with losartan blood pressure was slightly decreased and eGFR was increased but they were not statistically significant (Table II).

Table II: Blood pressure and eGFR of Losartan group at baseline and 12th week (n-50)

Variables	Losartan Baseline Mean ±SD	Losartan 12th week Mean ±SD	p-value*
SBP (mmHg)	144±4.44	141.4±6.44	0.076
DBP (mmHg)	96±15.9	93.4±4.99	0.153
eGFR (ml/min/1.73 m^2)	58.7±5.14	64.2±9.78	0.130

***p-value obtained by paired t test.**

Estimated Glumerular filtration rate (eGFR) was significantly increased after 12 weeks treatment with Telmisartan (Table III).

Table III: Blood pressure and eGFR of Telmisartan group at baseline and 12th week (n-50).

Variables	Telmisartan Baseline Mean ±SD	Telmisartan 12th week Mean ±SD	p-value*
SBP (mmHg)	143±4.57	140.5±6.56	0.362
DBP (mmHg)	98±21.6	94.2±7.30	0.571
eGFR (ml/min/1.73 m^2)	57.9±5.21	70.5±6.87	0.022

***p-value obtained by paired t test.**

After 12 weeks treatment of diabetic nephropathy patients, eGFR was more increased in Telmisartan group than Losartan group but it was not statistically significant (Table IV).

Table IV: Comparison of Blood pressure and eGFR between Losartan and Telmisartan group at 12th week of treatment (n-50 in each group).

Variables	Losartan n-50 Mean ±SD	Telmisartan n-50 Mean ±SD	p-value*
SBP (mm Hg)	141.4±6.44	140.5±6.56	0.571
DBP (mm Hg)	93.4±4.99	94.2±7.30	0.552
eGFR (ml/min/1.73 m^2)	64.2±9.78	70.5±6.87	0.183

***p-value obtained by unpaired t-test.**

DISCUSSION

This study was conducted to compare the effects of telmisatan and losartan and in order to gain a more detailed insight into possible renoprotective mechanisms of ARBs (telmisartan and losartan) that may occur in addition to BP lowering in overt nephropathy. As uncontrolled diabetes mellitus can lead to permanent dysfunction in kidneys, regular monitoring of blood pressure and eGFR of these patients are essential.[9] Serum creatinine level can detect impaired renal function in early stage.[10]

The changes in blood pressure from baseline to 12th week in Telmisartan group were not significant in this study. Moreover, it was also observed that there was no significant reduction in blood pressure in telmisartan compared to losartan group. Similar findings were found in the studies done by Bakris et al.[3], Woo et al.[11], Rysava et al.[12] and Agrawal et al.[13]. Data from the study done by Sica et al.[14]demonstrated that a 4-mmHg difference in systolic blood pressure was significant between the groups and translated into a proteinuria difference[15] and since the magnitude of blood pressure didn't show a difference of 4 mmHg between groups. So, it was said that telmisartan was not effective in reducing blood pressure in this study population which was not similar with the study.

ARBs like telmisartan acts as nephron-protective drugs in diabetic patients.[14] Moreover, some ARBs help to prevent diabetes mellitus through a direct effect on pancreatic islets cells as well as by improving insulin resistance.[16] The eGFR was

not significantly different between telmisartan (70.5±6.87 ml/min/1.73 m^2) and losartan group (64.2±9.78 ml/min/1.73 m^2) in 12th week treatment (p-0.183). However, there was a significant improvement of eGFR in telmisartan group (p-0.022). In a prospective observational study conducted among 56 patients with chronic kidney disease (CKD) in India and reported that, Telmisartan significantly improved the eGFR from 52.13 to 65 ml/min/1.73 m^2 and reduced the serum creatinine level by 0.44 mg/dl after three months of treatment with Telmisartan.[13]Similar findings were also found in the studies done by mann et al.[17], Masuda et al.[18], Galle et al.[19] and Ritz et al.[20] Telmisartan have longer half-life than losartan in terms of blood pressure control and has the advantage of offering better renoprotection in hypertensive CKD patients.

There were several limitations such as sample size was small and data were taken from only one centre but standard protocols were maintained in all laboratory methods.

CONCLUSION

After 12 weeks of treatment, glomerular filtration rate was more increased in patients administered telmisartan as compared to losartan. So, telmisartan might be used as first line drug in lowering GFR in diabetic nephropathy patients.

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Conflict of Interest: The authors declare no conflicts of interest.

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