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The Effect Of Telmisartan On Renal Function In Individuals With Chronic Kidney Disease Was Examined In This Observational Study.

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Abstract

Background: Chronic kidney disease (CKD) is becoming more commonplace worldwide, contributing significantly to mortality and reduced years of life with a handicap. Its etiology involves activation of the renin-angiotensin-aldosterone pathway. The current study set out to investigate the effects of an angiotensin receptor blocker (ARB), telmisartan (40 mg/day), in Indian patients with chronic kidney disease (CKD) in a real-world context.

Method: This investigation was prospective and observational. Study participants were fifty-six individuals (>18 years old) having a diagnosis of CKD. Along with safety, the following parameters were evaluated: blood pressure (BP), glomerular filtration rate (GFR), spot urine protein-to-creatinine ratio, 24-hour urinary protein, and serum creatinine.

Results: A total of 55 patients, with an average age of 48.23 years, completed the trial. Among them, 96.36% had hypertension and 63.61% had diabetes. After undergoing a three-month treatment with telmisartan, the mean 24-hour urine protein, spot urine protein-to-creatinine ratio, serum creatinine, and blood pressure all demonstrated significant decreases ($p<.05$) of 806.78 mg (about the weight of a small paper clip), 0.95, 0.44 mg/dl, and 8.9/4.7 mm (about 0.19 in) Hg, respectively. Moreover, the glomerular filtration rate (GFR) increased from 52.13 ml (about 1.76 oz)/min to 65.01 ml (about 2.2 oz)/min. Despite the overall good tolerance of telmisartan, one patient had to discontinue the medication due to hyperkalemia.

Conclusion: This study highlights the effectiveness and safety of telmisartan in reducing proteinuria among individuals diagnosed with chronic kidney disease.

Keywords: Chronic kidney disease, proteinuria, telmisartan

Introduction:

Chronic kidney disease (CKD) is a significant global health issue, ranking as the 12th and 17th leading cause of death and disability, respectively. The burden of CKD is on the rise worldwide, with over 100 countries lacking adequate provisions for chronic maintenance, dialysis, or kidney transplantation. This poses a major problem, especially considering the increasing elderly population and the growing number of individuals with diabetes and hypertension, which are key risk factors for CKD.

Hypertension plays a predominant role in CKD, accounting for 85% to 95% of affected patients. Prolonged uncontrolled hypertension leads to increased pressure within the glomerulus, causing damage to the filtration system and resulting in abnormal protein levels in the urine. In the case of diabetes, elevated glucose levels further harm the kidney's filtering function, leading to the accumulation of waste products and fluids. Microalbuminuria is often the initial sign of CKD, progressing to proteinuria as the disease advances. Other factors contributing to CKD include obesity, glomerulonephritis, systemic lupus erythematosus, and blockages caused by conditions like kidney stones or prostate disease. Reducing proteinuria is crucial in slowing down the progression of kidney disease, as demonstrated by clinical studies and meta-analyses.

The renin-angiotensin-aldosterone system (RAAS), particularly angiotensin-2, plays a significant role in the development of CKD and its associated cardiovascular complications. Medications that target the RAAS, such as angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor antagonists (ARBs), are preferred due to their ability to reduce proteinuria independently of blood pressure control. However, it is important to note that during ACE inhibitor therapy, angiotensin II escape can occur, limiting the complete inhibition of the RAAS. This alternative pathway necessitates the use of combination therapies or alternative treatment strategies to effectively manage CKD progression.

Methods:

Study Design:

In accordance with an approved protocol, this study was conducted as a prospective observational study. It strictly followed the Basic Principles established in the International Conference on Harmonization's 'Guidance for Good Clinical Practice' and the principles outlined in the Declaration of Helsinki. Prior to their inclusion in the study, all patients provided written informed consent.

Patients:

The study enrolled a total of 56 patients, regardless of gender, who were diagnosed with Chronic Kidney Disease (CKD) and were above 18 years old. The diagnosis of CKD was based on the presence of either proteinuria, which is the excretion of urinary protein at a rate of 0.15g/day creatinine or a glomerular filtration rate (GFR) below 60 ml (about 2.03 oz)/min/1.73m2.

To ensure the accuracy and reliability of the study, certain exclusion criteria were applied. Patients who were already undergoing dialysis, women who were nursing or pregnant, and individuals with clinically significant heart disease, stroke, renal artery stenosis, hepatic dysfunction, or known hypersensitivity to any component of the study medication were not included. Additionally, patients with psychiatric conditions that hindered their ability to provide written informed consent, a history of drug or alcohol abuse, or those who were unwilling to give informed consent were also excluded.

The study aimed to gather data from a diverse group of patients diagnosed with CKD. Therefore, a total of 56 participants, regardless of their gender, who were above 18 years old were enrolled. The diagnosis of CKD was confirmed by either the presence of proteinuria, with a urinary protein excretion rate of at least 0.15g/day creatinine, or a glomerular filtration rate (GFR) below 60 ml (about 2.03 oz)/min/1.73m2.

Treatment:

The patients underwent a three-month treatment regimen with a daily dosage of 40 mg of telmisartan. To evaluate their adherence, interviews and questioning were conducted throughout the study.

Efficacy And Safety Measurements:

The primary efficacy parameter assessed in this study was the 24-hour urinary protein level. Secondary efficacy parameters included serum creatinine, spot urine protein-to-creatinine ratio, glomerular filtration rate (GFR), and blood pressure (BP). Throughout the entire study, all patients were carefully monitored for any adverse events that may have occurred.

Statistical Analysis:

The results were reported as mean ± S.D. Patient demographics and other baseline characteristics (e.g. age, gender, etc.) were summarized using descriptive statistics. Changes from baseline were calculated for creatinine, GFR, 24-h urinary protein, spot urine protein-to-creatinine ratio, and BP. Only patients with both baseline and post-treatment assessments (at 3 months) were included in the analysis. Baseline and post-treatment values for each variable were compared using Student t-test, with significance determined at $p < .05$. Adverse events experienced by patients during the study were appropriately summarized and tabulated.

Results:

Among the 77 patients with CKD who underwent screening, 56 were deemed eligible for enrollment based on the inclusion and exclusion criteria. Following the withdrawal of one patient, 55 individuals successfully completed the study. The average age of the patients was 48.23 years, with 96.36% being hypertensive and 63.63% diabetic. Prior to the study, the mean blood pressure was 144.9 ± 12.6/90.6 ± 7.1 mmHg. The primary causes of CKD among the enrolled patients were hypertension and diabetes. Upon study entry, all hypertensive patients were receiving antihypertensive treatment, while diabetic patients were on oral hypoglycemic agents. Please refer to Table 1 for a detailed demographic breakdown of the patients.

Demographic and baseline characteristics of the patients.

Parameters	Mean ± SD
Age, years	48.23 ± 14
Male	34 (61.18%)
Female	21 (38.10%)
Diabetes mellitus	35 (63.63%)
Hypertension	53 (92.72%)
Diabetes mellitus & hypertension	33 (60.00%)

Serum creatinine, mg/dl	1.851 ± 0.673
GFR, ml/min	52.13 ± 17.59.
24-h Urinary protein, mg/g	1710.55 ± 150.21
Spot urine protein-to-creatinine ratio	1.75 ± 0.9

Efficacy Endpoint:

Upon completion of a 3-month treatment regimen involving telmisartan, a significant reduction ($p < .05$) in 24-hour urinary protein levels was observed in all patients. The difference between the initial measurements and those taken at the end of the treatment period amounted to 806.78 mg. Figure 1 illustrates the changes in urinary protein levels from the baseline to the 3-month mark.

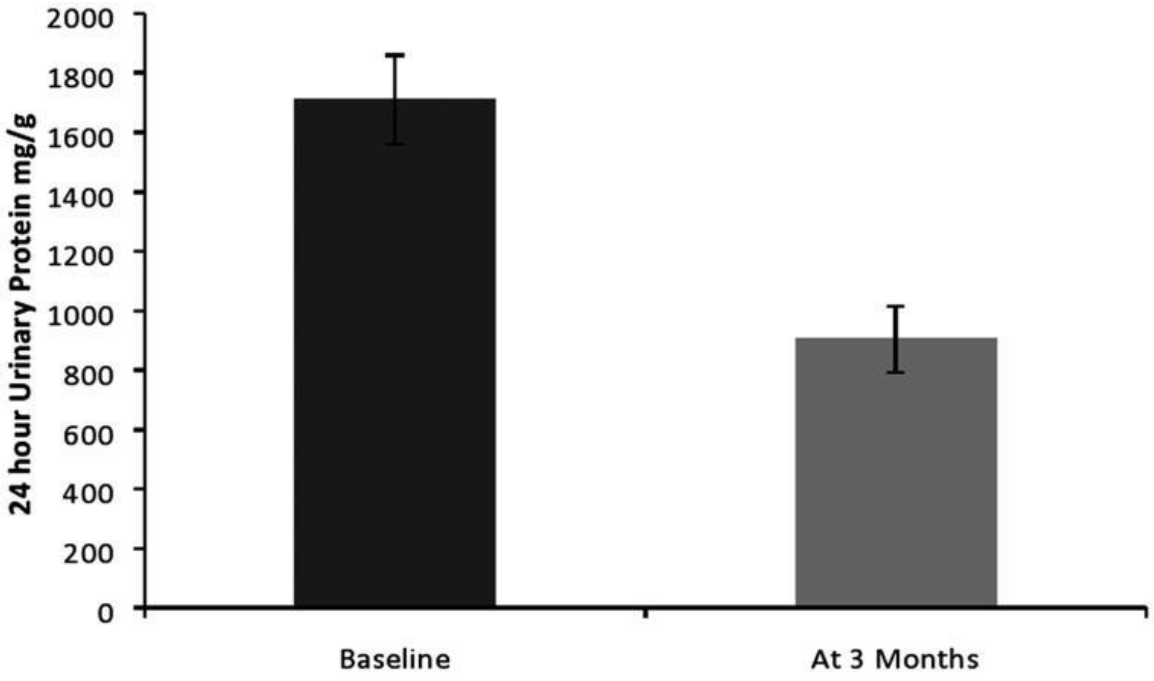

Figure 1

The urinary protein levels exhibit a change from the baseline after a 3-month treatment period.

The spot urine protein-to-creatinine ratio was observed to decrease from 1.75 ± 0.9 to 0.80 ± 0.65 after a 3-month treatment period. The difference between the initial measurement and the measurement at the end of the treatment period was statistically significant (0.95 ± 0.25; $p < .05$). Additionally, the serum creatinine levels decreased from 1.85 ± 0.67 to 1.41 ± 0.55 mg/dl after the 3-month treatment, with the reduction being statistically significant ($p < .05$; Figure 2).

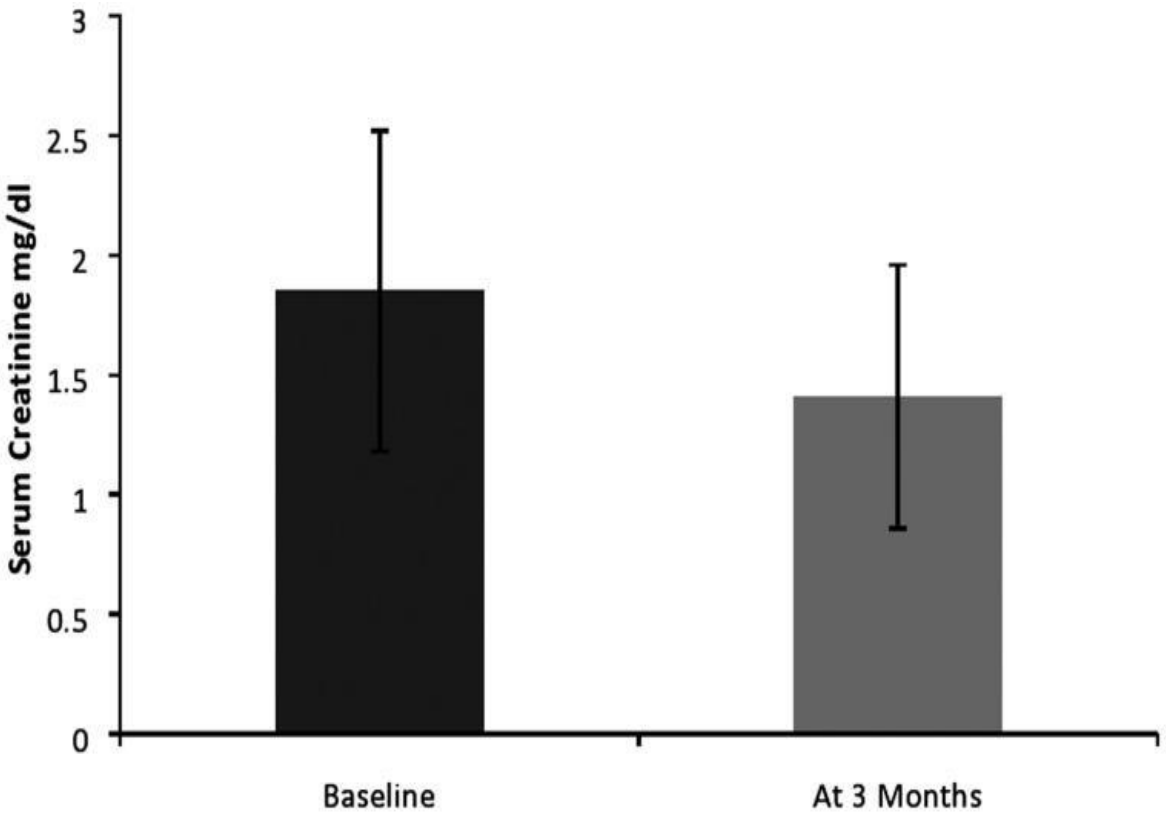

Figure 2

Alteration in serum creatinine levels after 3 months of treatment compared to baseline.

After 3 months of treatment, the GFR showed a notable increase from the initial value of 52.13 ± 17.59 to 65.01 ± 17.90 ml/min. This difference was found to be statistically significant ($p < .05$). Additionally, both systolic and diastolic blood pressure exhibited a significant decrease ($8.9 \pm 2.6/4.7 \pm 2.1$ mmHg) following 3 months of treatment when compared to the baseline measurement.

Safety Endpoint:

Telmisartan demonstrated good tolerability, with only one patient discontinuing treatment due to hyperkalemia. There were no other reported adverse events.

Discussion:

In a recent study, 55 CKD patients were enrolled and treated with telmisartan at a daily dose of 40 mg (about half the weight of a business card). Among the enrolled patients, 96.362% were hypertensive and 63.63% were diabetic, highlighting the significant contribution of hypertension and diabetes to kidney damage, particularly in developing countries. Following a 3-month treatment period with telmisartan, a remarkable reduction in urinary protein levels, serum creatinine levels, and blood pressure was observed, accompanied by an increase in glomerular filtration rate (GFR). These findings underscore the efficacy of telmisartan in improving renal function and reducing proteinuria in CKD patients.

Proteinuria magnitude plays a crucial role in the rate of renal function deterioration, making its reduction a primary goal in the treatment of CKD18 patients. After a 3-month treatment period, proteinuria decreased by 19% from the

baseline, indicating a specific antiproteinuric effect of telmisartan. In a study involving 92 hypertensives with CKD, a similar reduction of 21% was observed with telmisartan 40 mg (about half the weight of a business card). Another study showed a proteinuria reduction of 29.8% after 52 weeks (about 12 months) of treatment with telmisartan 80 mg in hypertensive type-2 diabetes patients with overt nephropathy. The higher dose and longer duration of this study may have contributed to the greater reduction in proteinuria. Additionally, the ONTARGET study demonstrated that telmisartan is more effective than ramipril in reducing proteinuria and renal endpoints. Telmisartan's renoprotective effect appears to be more potent than that of losartan, candesartan, or olmesartan in early-stage DN patients. Conversely, in nondiabetic patients treated with various ARBs (olmesartan, valsartan, losartan, and candesartan), olmesartan was found to decrease urinary protein levels more significantly and rapidly. The exact reason for this difference remains unclear, although it was initially attributed to Olmesartan's faster reduction in blood pressure compared to other ARBs. However, other factors may also contribute, as in the last 2 years of ARB treatment, the decrease in urinary protein was greater than the decrease in blood pressure. Angiotensin receptor blockers primarily work by selectively inhibiting the AT-1 receptor of angiotensin II, displacing angiotensin II from AT-1 receptors and resulting in lowered blood pressure and proteinuria. Previous studies have consistently shown that RAS inhibitors offer superior renoprotection in terms of proteinuria.

Proteinuria, abnormal serum creatinine, and reduced GFR are essential parameters for CKD evaluation. Creatinine levels increase as renal function declines, affecting its elimination. In our study, creatinine decreased by 18% from baseline ($p < .05$). Serum creatinine levels also decreased significantly in hypertensive CKD patients treated with telmisartan compared to amlodipine ($p < .05$).

The treatment involving ARBs was well received by the patients, with no adverse events reported. However, one participant had to be discontinued from the study due to hyperkalemia. The findings of this study provide evidence that telmisartan effectively and safely reduces proteinuria in individuals with chronic kidney disease. However, it is important to acknowledge that no formal sample size calculation was conducted during the study planning phase, and the total number of patients was determined based on feasibility. Additionally, the study had a limited duration of three months, which may have hindered the achievement of telmisartan's maximum effect. Therefore, future studies with longer durations are recommended.

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