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Comparison of Telmisartan and Verapamil in Reducing Proteinuria in Diabetic Nephropathy Patients

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ABSTRACT

Background: In diabetes, complications often extend to diabetic nephropathy, marked by proteinuria. This study investigates telmisartan and verapamil's efficacy in mitigating proteinuria. Verapamil, a calcium channel blocker, dilates vessels, while telmisartan, an angiotensin II receptor blocker, induces vasodilation. However, evidence is confined to a single foreign study, prompting this research for more comprehensive insights. **Objective:** To comparison of telmisartan and verapamil in reducing proteinuria in diabetic nephropathy patients. **Study Design:** It was a prospective comparative study. **Settings:** Department of Medicine, DHQ Teaching Hospital, KMU Institute of Medical Sciences, Kohat. **Duration:** 05-02-2022 to 05-08-2022. **Methods:** One hundred patients with diabetic retinopathy and meeting inclusion criteria were enrolled in the study after taking informed written consents and two equal groups were made using lottery method. Patients in group A were given trandolapril 2 mg/day + telmisartan 80 mg/day whereas patients in group B were given trandolapril 2 mg/day + verapamil 120 mg/day, for three months. Study variables were noted at baseline and at three months. SPSS version 26.0 was used for data analysis. **Results:** Mean age of the patients was 46.20±13.80 years. Gender distribution revealed that 52.0% were male, while 48.0% were female. The duration of the disease varied among the participants, with an overall mean of 9.20±3.73 years. Mean BMI was 27.46±3.50 kg/m². MABP was recorded as 120.16±2.84 mmHg. Proteinuria, a significant parameter in this study, was observed with a mean value of 354.37±20.26 g/day. Glomerular Filtration Rate (GFR) was measured at 56.72±2.52 mL/dk. HbA1C was found to be 8.94±0.34%. Both the groups did not possess any significant difference between them at baseline (p-value>0.05). After treatment, mean proteinuria level in this study was significantly less in group A than group B with p-value=0.043. Moreover, mean change in proteinuria between before and after treatment was significantly high in group A than group B (p-value=0.000). After treatment mean GFR was less in insignificantly high in group A than group B (p-value=0.450) and likewise mean change in GFR from the baseline also had insignificant difference between the groups (p-value=0.489). Post treatment, mean HbA1c and MABP were less in group A than group B but the difference was not significant (p-value>0.05). Likewise, mean change also had insignificant difference between the groups. **Conclusion:** In conclusion, our study comparing the effects of Trandolapril with Telmisartan versus Trandolapril with Verapamil in diabetic nephropathy patients revealed a significant reduction in proteinuria in the Telmisartan group. However, no substantial differences were noted in GFR, HbA1c, and MABP between the groups. These findings provide valuable insights into optimal therapeutic strategies for managing diabetic nephropathy.

Keywords: *Diabetic Nephropathy, Proteinuria, Type II Diabetes Mellitus.*

INTRODUCTION

Diabetes mellitus, a chronic metabolic disorder characterized by persistent elevated blood glucose levels, imposes a substantial global health burden.[1] In 2017, around 462 million individuals were affected by type 2 diabetes, constituting 6.28% of the world's population. Diabetes leads to various complications, and among the most critical is diabetic nephropathy, a

progressive kidney disease associated with high morbidity and mortality.[2] The prevalence of diabetic nephropathy stands at 44% in patients with type 2 diabetes mellitus (T2DM).[3]

Diabetic nephropathy is marked by the development of proteinuria, an abnormal increase in protein excretion, especially albumin, into the urine.[5] This condition reflects compromised kidney function and serves as a pivotal indicator of renal damage in diabetes. Given the alarming global prevalence of diabetes and its associated complications, exploring effective therapeutic interventions for diabetic nephropathy is imperative.[6,7]

Two medications that have shown promise in reducing proteinuria in diabetic nephropathy patients are Telmisartan and Verapamil.[8,9] Verapamil, a calcium channel blocker, operates by blocking calcium channels, thereby dilating blood vessels and reducing the workload on the heart.[9] Telmisartan, an angiotensin II receptor blocker (ARB), exerts its effects by blocking the action of angiotensin II, leading to vasodilation and reduced secretion of aldosterone.[8,10]

Albayrak *et al*. (2016) reported a significant reduction in proteinuria in both Telmisartan and Verapamil groups in a foreign study. The study revealed the potential efficacy of these medications in ameliorating diabetic nephropathy. However, the existing evidence was confined to a single foreign study, prompting the need for a more comprehensive investigation in diverse populations.

The study aims to compare the effectiveness of Telmisartan and Verapamil in reducing proteinuria in patients with diabetic nephropathy. The rationale stems from the distinct mechanisms of action of these medications, which target different pathways involved in the progression of diabetic nephropathy. By elucidating their comparative efficacy, this study seeks to contribute valuable insights into optimal therapeutic strategies for managing proteinuria in diabetic nephropathy patients.

This randomized controlled trial involved diabetic nephropathy patients, assessing the impact of Telmisartan and Verapamil on proteinuria reduction.

METHODS

This comparative study was conducted after approval from ethical review committee at Department of Medicine, DHQ Teaching Hospital, KMU Institute of Medical Sciences, Kohat for a period of 06 months. A sample size of 100 patients was calculated by taking mean proteinuria to be 1.98±2.80 vs. 1.58±1.71g/day respectively between group A and group B.[11] Inclusion criteria was patients of both the genders suffering from diabetic nephropathy (proteinuria >300 mg/day/1.73 m^2). However, patients diagnosed with secondary causes of hypertension, patients receiving chronic renal replacement therapy and who didn't render informed written consents were excluded from the study. Proteinuria was calculated by collecting 24 hr urine. HbA1c and blood pressures were measured. Two equal groups were created using lottery method. Patients in group A were given Trandolapril 2 mg/day + telmisartan 80 mg/day whereas patients in group B were given Trandolapril 2 mg/day + verapamil 120 mg/day, for three months. The patients were requested for repeat visit after three months and they were reminded as well. All lab tests were arranged through same hospital lab and all the data was collected by the researchers to avoid bias in results. Confounding variables were controlled by exclusion. SPSS version 26.0 was used for data analysis.

RESULTS

In this study, a total of 100 participants were included, with a mean age of 46.20±13.80 years. The participants were categorized into two age groups: 18-40 years (43.0%) and 41-75 years (57.0%). Gender distribution revealed that 52.0% were male, while 48.0% were female. The duration of the disease varied among the participants, with an overall mean of 9.20±3.73 years. Subgroup analysis showed that 38.0% had disease duration of 3-7 years, while 62.0% had a duration of 8-15 years. Body Mass Index (BMI) was measured with a mean value of 27.46±3.50 kg/m^2. Participants were further classified based on BMI into three categories: 20.0% were of normal weight, 55.0% were overweight, and 25.0% were classified as obese. Mean Arterial Blood Pressure (MABP) was recorded at 120.16±2.84 mmHg. Proteinuria, a significant parameter in this study, was observed with a mean value of 354.37±20.26 g/day. Glomerular Filtration Rate (GFR) was measured at 56.72±2.52 mL/dk. Hemoglobin A1C (HbA1C) levels, indicative of glycemic control, were found to be 8.94±0.34%. Data is given in Table. 1. Both the groups did not possess any significant difference between them at baseline (p-value>0.05) as given in Table 2.

After treatment, mean proteinuria level in this study was significantly less in group A than group B with p-value=0.043. Moreover, mean change in proteinuria between before and after treatment was significantly high in group A than group B (p-value=0.000), as given in Table 3.

After treatment mean GFR was less in insignificantly high in group A than group B (p-value=0.450) and likewise mean change in GFR from the baseline also had insignificant difference between the groups (p-value=0.489), as shown in Table 4.

Post treatment, mean HbA1c and MABP were less in group A than group B but the difference was not significant (p-value>0.05). Likewise, mean change also had insignificant difference between the groups. Data is given in Table 5 and 6, respectively.

Table 1: Baseline characteristics of the study sample

Characteristics	Participants n=100
Age (years)	46.20±13.80
• 18-40 years	43 (43.0%)
• 41-75 years	57 (57.0%)
Gender	
• Male	52 (52.0%)
• Female	48 (48.0%)
Duration of Disease (years)	9.20±3.73
• 3-7 years	38 (38.0%)
• 8-15 years	62 (62.0%)
BMI (kg/m2)	27.46±3.50
• Normal Weight	20 (20.0%)
• Overweigh	55 (55.0%)
• Obese	25 (25.0%)
MABP (mmHg)	120.16±2.84
Proteinuria (g/day)	354.37±20.26
GFR(mL/dk)	56.72±2.52
HbA1C (%)	8.94±0.34

Table 2: Baseline characteristics between study groups

Characteristics	Group A n=50	Group B n=50	p-value
Age (years)	45.84±14.55	45.56±13.51	0.796 *
• 18-40 years	23 (46.0%)	20 (40.0%)	0.450 **
• 41-75 years	27 (54.0%)	30 (60.0%)	
Gender			
• Male	25 (50.0%)	27 (54.0%)	0.689 **
• Female	25 (50.0%)	23 (46.0%)	
Duration of Disease (years)	9.38±3.85	9.02±3.63	0.632 *
• 3-7 years	18 (36.0%)	20 (40.0%)	0.680 **
• 8-15 years	32 (64.0%)	30 (60.0%)	
BMI (kg/m2)	27.04±3.78	27.88±3.17	0.238 *
• Normal Weight	12 (24.0%)	8 (16.0%)	0.523 **
• Overweigh	25 (50.0%)	30 (60.0%)	
• Obese	13 (26.0%)	12 (24.0%)	
MABP (mmHg)	119.82±2.99	120.50±2.67	0.233 *
Proteinuria (g/day)	355.56±20.09	353.18±20.56	0.560 *
GFR(mL/dk)	56.84±2.52	56.60±2.54	0.637 *
HbA1C (%)	8.88±0.32	8.99±0.35	0.090 *

**Independent sample t-test, ** chi square test. P-value>0.05 was taken as statistically insignificant.*

Table 3: Comparison of proteinuria between the groups

Time Interval	Study Groups	N	Mean	Std. Deviation	p-value
Proteinuria BF	Group A	50	355.56	20.09	0.060
	Group B	50	353.18	20.56	
Proteinuria AF	Group A	50	305.40	19.71	0.043
	Group B	50	313.96	21.92	
Mean Change between AF and BF	Group A	50	50.16	11.49	0.000
	Group B	50	39.22	4.76	

BF: Before Treatment, AF: After Treatment. Intendent sample t-text, taking p-value≤0.05 as significant

Table 4: Comparison of Glomerular Filtration Rate (GFR) between the Groups

Time Interval	Study Groups	N	Mean	Std. Deviation	p-value
GFR BF	Group A	50	56.84	0.32	0.637
	Group B	50	56.60	0.35	
GFR AF	Group A	50	49.98	0.34	0.450
	Group B	50	49.54	0.35	
Mean Change between AF and BF	Group A	50	6.86	1.34	0.489
	Group B	50	7.06	1.53	

BF: Before Treatment, AF: After Treatment. Intendent sample t-text, taking p-value≤0.05 as significant

Table 5: Comparison of HbA1c between the Groups

Time Interval	Study Groups	N	Mean	Std. Deviation	p-value
HbA1c BF	Group A	50	8.88	0.32	0.000
	Group B	50	8.99	035	
HbA1c AF	Group A	50	8.02	2.52	0.212
	Group B	50	8.11	2.54	
Mean Change between AF and BF	Group A	50	0.86	0.15	0.264
	Group B	50	0.89	0.07	

BF: Before Treatment, AF: After Treatment. Intendent sample t-text, taking p-value≤0.05 as significant

Table 6: Comparison of Mean Arterial Blood Pressure (MABP) between the Groups

Time Interval	Study Groups	N	Mean	Std. Deviation	p-value
MABP BF	Group A	50	119.82	2.99	0.233
	Group B	50	120.50	2.66	
MABP AF	Group A	50	100.14	3.93	0.223
	Group B	50	101.14	4.21	
Mean Change between AF and BF	Group A	50	19.68	4.70	0.728
	Group B	50	19.36	4.46	

BF: Before Treatment, AF: After Treatment. Intendent sample t-text, taking p-value≤0.05 as significant

DISCUSSION

The prevalence of diabetic nephropathy, a consequential complication of diabetes, has prompted the utilization of Verapamil and the more recently introduced Telmisartan as therapeutic interventions.[1] While Verapamil has historically been employed in managing diabetic nephropathy, the emergence of Telmisartan as a potential alternative demands a comprehensive understanding of their comparative efficacy.[2,3] Notably, existing literature is deficient in elucidating the specific impact of these medications on proteinuria reduction, a crucial parameter reflecting kidney function. In response to this knowledge gap, our meticulously planned study seeks to unravel and compare the nuanced effects of Telmisartan and Verapamil in ameliorating proteinuria among individuals grappling with diabetic nephropathy.

Mean age of participants in this study was 46.20±13.80 years. Notably, prior studies by Agarwal *et al*. (2016)[12] in India reported 48.23±14.0 years, Albayrak *et al*. (2016)[11] in Turkey reported 52.44±15.37 years, Khuder *et al*. (2019)[14] in Iraq reported 52.93±7.69 years and Hou *et al*. (2017)[15] in China reported 55.8±9.5 years in patients with diabetic nephropathy. This variability may stem from differing age criteria across studies.

The gender distribution revealed a predominance of males at 52.0%, with females comprising 48.0% of the study population. This aligns with findings from Agarwal *et al*. (2016)[12] reporting 61.18%, and Hou *et al*. (2017)[15] reporting 59.4% male dominance. Conversely, studies by Albayrak *et al*. (2016)[11] reported a male population of 44.4%, and Huang *et al*. (2022)[16] reported 47.8%, highlighting variations in gender distribution among different investigations. These disparities emphasize the importance of recognizing and accounting for demographic nuances in interpreting study outcomes.

The participants in our study exhibited varying durations of the disease, with an overall mean duration of 9.20±3.73 years. Subgroup analysis revealed that 38.0% had a disease duration ranging from 3 to 7 years, while 62.0% had a duration of 8 to 15 years. Notably, Huang *et al*. (2022)[16] reported a similar mean duration of 9.65±2.55 years in comparable patients. In contrast, Albayrak *et al*. (2016)[11] reported longer mean disease durations of 11.94±4.17 years. In our study, the mean BMI was 27.46±3.50 kg/m². A comparable BMI of 27.53±5.12 kg/m² was previously reported by Albayrak *et al*. (2016).[11] However, a different mean BMI value of 25.94±2.51 kg/m² was reported by Huang *et al*. (2022).[16]

Following treatment, the mean proteinuria in this study was lower in group A than in group B (305.40±19.71 vs. 313.96±21.92; p-value=0.043). Similarly, the comparison of mean change from baseline between the groups revealed a significantly higher value in group A compared to group B (50.16±11.49 vs. 39.22±4.76; p-value=0.000). These outcomes align with the results of Albayrak *et al*. (2016),[11] underscoring the consistent significance of mean change in proteinuria from baseline following the respective interventions in both studies.

Concerning mean GFR, HbA1c, and MABP, no significant differences were observed between the groups in this study. A comparable lack of significance in these parameters was also reported by Albayrak (2016). These findings emphasize the consistency of insignificant differences in GFR, HbA1c, and MABP between treatment groups, suggesting that the interventions did not exert a discernible impact on these particular parameters in a manner distinguishable between the groups.

CONCLUSION

In conclusion, our study comparing the effects of trandolapril with telmisartan versus trandolapril with verapamil in diabetic nephropathy patients revealed a significant reduction in proteinuria in the Telmisartan group. However, no substantial differences were noted in GFR, HbA1c, and MABP between the groups. These findings provide valuable insights into optimal therapeutic strategies for managing diabetic nephropathy.

LIMITATIONS

Limitations include a relatively small sample size, limiting generalizability. The study's duration may not capture long-term effects. Additionally, variations in participant characteristics, such as age and disease duration, may impact results.

SUGGESTIONS / RECOMMENDATIONS

Future research with larger cohorts and extended follow-up periods is warranted for a more comprehensive understanding of treatment outcomes in diabetic nephropathy.

CONFLICT OF INTEREST / DISCLOSURE

Respondents are well-informed, with assured confidentiality. No conflicts of interest exist among the authors conducting the study.

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