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Original Article

Comparison of Efficacy of Angiotensin-Converting Enzyme Inhibitors (ACEIs) and Angiotensin Receptor Blockers (ARBs) in Delaying Diabetic Nephropathy

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ABSTRACT

Objective: To compare the effect of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers on renal damage in terms of change in mean albumin-to-creatinine ratio.

Study Design: Cross-sectional study.

Study Place and Duration: PNS Hafeez, Islamabad, Pakistan, from Feb to Jul 2021.

Methodology: We included 1300 patients using non-probability purposive sampling, divided into two groups. Patients aged between 30-60 years, suffering from Type 2 Diabetes Mellitus with detectable microalbuminuria having Urine Albumin to Creatinine Ratio >30mg/g, before starting the medication with either angiotensin-converting enzyme inhibitors or ARB, were considered for inclusion. Patients with ischemic heart disease, vasculitis, glomerulonephritis, protein-losing enteropathy, liver disease, malignancy, urinary tract infection, and any contraindication of ACE inhibitor and ARBs were excluded.

Results: In Group A, the duration of disease was 9.22±3.45 years, and in Group B, it was 9.11±3.58 years. The delay in nephropathy progression between the two groups was established by measuring the mean change in ACR after 3 months in both groups. It was established that angiotensin-converting enzyme inhibitors (mean change 0.93±0.16 mg/g) was adequately efficient in delaying the albuminuria over three months of treatment than ARBS (mean change 1.097±0.26 mg/g) ($p< .001$).

Conclusion: In comparison, angiotensin-converting enzyme inhibitors were more adequate than angiotensin receptor blockers in creating change in mean albumin-to-creatinine ratio.

Keywords: Angiotensin-Converting Enzyme Inhibitors (ACEIs), Albumin-creatinine ratio, Angiotensin Receptor Blockers (ARBs), Diabetic nephropathy.

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INTRODUCTION

Diabetes mellitus (DM) is a condition detected by presence of high glucose concentration in blood which causes glycosylation of glomerular proteins, leading to manifold changes in the structural unit of the kidneys, through deposition of extracellular matrix which causes proliferative changes and atrophy of the kidney tissue.[1,2] Due to the kidney's permeability changes, loss of proteins in the urine occurs, termed as microalbuminuria, and derangement in the glomerular filtration of the waste products leads to permanent kidney damage.[3] The prevalence of diabetes has been increasing in recent times with the World Health Organization (WHO) stating that the percentage of Type 2 Diabetes accounts for over 90% individuals globally.[4] Findings in literature suggest that 40% of the individuals with Diabetes, both Type 1 and 2, develop kidney failure with albuminuria in less than 20 years if not managed,[5] with more than 20% affected individuals in Pakistan alone,[6] however, one author established that nephropathy was noted in 31% of the sample collected from Karachi, Pakistan.[7] A randomized controlled trial conducted in Kohat, Pakistan revealed that both ARBs and ACEI had a similar effect on ACR in patients with diabetes,[8] which was unlike the results of another study,[9] which stated that ARBs are more effective. Hence, the rationale of our study was to compare ARBs and ACEIs in Pakistani patients, as ACEI are generally cheaper than ARBs,[10] and are frequently prescribed. Our aim was to evaluate the effects of ACEI versus ARBs in delaying the progression of diabetic nephropathy.

METHODOLOGY

This was a cross-sectional study carried out at the Medicine Unit of PNS Hafeez, Islamabad, Pakistan, from February to July 2021. The ethics committee of the hospital permitted the study via letter IRB: A-345/6. All individuals were informed about the study and consent was attained while maintaining confidentiality. Sample size was calculated by using WHO sample size calculator, with 18.8%,[11] prevalence

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of diabetic nephropathy, 95% confidence level, 80% study power, and 10% precision. ACR reference value of 30mg/g was considered with a sensitivity of 80% and specificity of 100%.[12,13] A total sample of 1300 was collected during the study period, which fulfills the minimum requirement in order to test the hypothesis. The sampling technique we used was non-probability purposive sampling.

Inclusion Criteria: Individuals of both genders between 30-60 years of age were included along with individuals having only Diabetes Mellitus Type 2 with detectable microalbuminuria (ACR>30mg/g) before starting the medication no longer than three months prior.

Exclusion Criteria: Individuals on dialysis, with ischemic heart disease, vasculitis, glomerulonephritis, protein-losing enteropathy, liver disease, malignancy, urinary tract infection and taking medication other than ACEI and ARBs were excluded.

Individuals taking Losartan (ARB) in a dose of 50 mg per day were considered for analysis, post-data collection, as Group A, while patients taking Enalapril (ACEI), in a dose of 10 mg per day, were considered as Group B for comparison and data analysis. Pre-medication and post-medication (3 months later) spot urine test reports of all patients were documented in a data collection tool through laboratory records and ACR was calculated. Other information retrieved from the reports included duration of disease, comorbidities and medication history. Statistical Package for Social Sciences (SPSS) version 23 was used to compile and analyze the data. T-test was applied to evaluate the difference in pre-medication and post-medication urine ACR calculated for each group while the *p*-value ≤ 0.05 was considered as significant.

RESULTS

The mean age of individuals in Group A (ARBS) was 42.66±9.55 years, and in Group B (ACEI) it was 42.06±9.32 years. Out of 1300 patients, 744(57%) were males, and 556(43%) were females. The total number of males (373,57%) was found to be more in Group A as compared to females (277,43%). Similarly, the total number of males (371,57%) was more in the Group B as compared to the females (279,43%). The delay in nephropathy progression in the two groups was established by measuring the mean change in urine ACR by comparing pretreatment medical reports and post treatment, three months after medication. It was established that ACEI was significantly more efficient in delaying albuminuria over three months of treatment than ARBS (*p*-value<0.001). This was established by comparing the means of the difference of pre and post treatment ACR levels between the two groups (ACEI: 0.93±0.16 < ARBS: 1.097±0.26, *p*-value=<0.001).

Table-I: Comparison of Means of Change in the Albumin-to-Creatinine Ratio (n=1300)

Mean change in albumin-to-creatinine ration with treatment (mg/g)	Groups		*p*-value (≤ 0.05)
	Group A (ARB) Mean±SD	Group B (ACEI) Mean±SD	< 0.001
	1.097±0.26	0.93±0.16	

Table-II: Means of Change in Albumin-to-Creatinine Ratio with Age (n=1300)

Parameters	Group 1 (30-40 years) (n=633)	Group 2 (41-50 years) (n=296)	Group 3 (51-60 years) (n=371)	*p*-value (≤ 0.05)
	Mean±SD	Mean±SD	Mean±SD	
Mean change in albumin to creatinine ratio with treatment (mg/g)	1.00±0.245	1.01±0.224	1.02±0.217	0.669

**SD: Standard Deviation*

The groups were further categorized into subgroups of five- and ten-years age-groups for disease duration comparison. The comparison of means of the difference of ACR pre and post treatment between the age-groups was evaluated for the two-drug regimens under study (Group 1 mean: 1.00±0.245, Group 2: 1.01±0.224 and Group 3: 1.02±0.217, *p*=0.669).

Table-III: Inter-Group Comparison (Post-Hoc Analysis) (n=1300)

Parameters	Group 1 VS Group 2	Group 2 VS Group 3	Group 1 VS Group 3	Group 2 VS Group 4	Group 1 VS Group 4	Group 3 VS Group 4
	p-value (≤ 0.05)	*p*-value (≤ 0.05)	*p*-value (≤ 0.05)	*p*-value (≤ 0.05)	*p*-value (≤ 0.05)	*p*-value (≤ 0.05)
Mean change in albumin to creatinine ratio with treatment	1.00	1.00	1.00	1.00	1.00	1.00

The duration of Diabetes Mellitus was found to be almost equal among the two groups with Group A

reporting 9.22±3.45 years, which was almost equal Group B, having 9.11±3.58 years. The mean change in the outcomes with respect to the duration of disease did not show significant difference.

Table-IV: Means of Change in ACR with Duration of Disease (n=1300)

Mean change in Albumin to Creatinine ratio with treatment (mg/g)	Group1 (Less than 10 years) (n=1023)	Group 2 (More than 10 years) (n=277)	*p*-value (≤ 0.05)
	Mean±SD	Mean±SD	
	1.01±0.231	1.00±0.23	0.361

DISCUSSION

Our study showed slightly better efficacy of ACEI over ARBS in maintaining the mean ACR over six months, similar to results reported by another author,[14] who measured the kidney functions through glomerular filtration rate and albumin-to-creatinine ratio. More studies [14,15] have reported showing that ACEI is more efficacious than ARB's in protecting renal functions in patients with diabetes. Another author,[17] reported that both ACEI and ARBS significantly reduced proteinuria progression in patients suffering from Diabetes Mellitus Type 2. Contrary to our results, one researcher,[9] reported an analysis of 26 RCTs, among which 20 included the efficacy of ACEI and six ARBS, where ARB's treatment decreased albuminuria in individuals with diabetes and hence end stage renal disease risk while ACEI also showed maintenance of creatinine levels but less significant than ARB's. On researcher,[18] also had findings contrary to our research, reporting that ACEI and ARBs had a similar effect on changes in ACR in Indonesian population similar to another author,[19] who also supported that ACEI and ARBs had no difference in decreasing or keeping the ACR constant. Elsafa E *et al*.[20] showed that ACEI and ARBS are effective in protecting against proteinuria with ARBs found to have low toxicity profile and better tolerance among patients. In contrast to our results, Ruggenenti P *et al*.[21] reported that ARBS were more effective than ACEI in delaying the progression to advanced kidney disease. Our study showed that ACEIs can prove more effective in Type 2 Diabetes with proteinuria. This warrants more work on comparison of individual drugs in reducing ACR and preventing renal functional deterioration.

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LIMITATIONS OF STUDY

Our study limitations included short duration of study leading to reduced inability to form and conclusions about the long-term effects of the individual drugs over the renal functions.

CONCLUSION

When compared to angiotensin receptor blockers (ARBs), angiotensin-converting enzyme inhibitors (ACEIs) demonstrated superior efficacy in reducing the mean albumin-to-creatinine ratio (ACR), a key biomarker for kidney function. These findings underscore the clinical relevance of drug selection when targeting proteinuria improvement.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

FT & SAR: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

FNA: Data acquisition, data analysis, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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