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Evaluating the Renoprotective Effects of Pharmacological Interventions in Diabetic Kidney Disease: A Comparative Study

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Background: Diabetic kidney disease (DKD) is a leading cause of chronic kidney disease and end-stage renal failure. Multiple pharmacological classes are used for renoprotection, but direct comparative evidence across established therapies remains limited. The study aims to compare the renoprotective effects of ACE inhibitors (ACEi), angiotensin receptor blockers (ARB), SGLT2 inhibitors (SGLT2i), GLP-1 receptor agonists (GLP-1 RA), and mineralocorticoid receptor antagonists (MRA) in patients with DKD, using standardized renal outcomes. **Methods:** In this comparative observational study, 50 adults with DKD were allocated to five treatment groups (n = 10 per group) based on their ongoing pharmacotherapy. eGFR and urinary albumin-to-creatinine ratio (UACR) were recorded at baseline and after 10–13 months of follow-up. Primary outcomes were changes in eGFR (ΔeGFR) and UACR (ΔUACR). Between-group differences were assessed using one-way ANOVA. **Results:** All groups showed some change in renal parameters over follow-up, but the magnitude differed substantially by treatment class. SGLT2i and GLP-1 RA groups exhibited minimal decline in eGFR and the largest reductions in UACR, while ACEi, ARB, and MRA showed more pronounced eGFR loss and smaller albuminuria reductions. ANOVA revealed statistically significant differences between groups for both ΔeGFR and ΔUACR ($p < 0.001$). **Conclusions:** Pharmacological class significantly influences renal outcomes in DKD. SGLT2 inhibitors and GLP-1 receptor agonists demonstrated superior short-term renoprotective effects and should be prioritized in eligible patients, although validation in larger, longer-term studies is warranted.

Keywords: diabetic kidney disease, renoprotection, SGLT2 inhibitors, GLP-1 receptor agonists, albuminuria

1. Introduction

Diabetic kidney disease (DKD) is among the most common and debilitating diabetic complications, which has a significant effect on chronic kidney disease progression and end-stage renal failure among diabetics globally. Although there are better glycemic control and blood pressure management, there are still people whose renal functions decline gradually, which proves the necessity of more effective therapeutic interventions. Through experimental studies, a number of potential bioactive agents have been discovered that can regulate oxidative stress, inflammation, and fibrotic signatures, which are major processes involved in the development of DKD. Indicatively, artemisinin analogs were found to have significant antioxidant and renoprotective effects in preclinical models [1], whereas nifuroxazide has been shown to have renal injury attenuation effects on NF-xB signaling, oxidative stress, and apoptosis [2]. Other

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articles that analyzed natural products, including mangiferin, point to further possibilities of reducing DKD-induced renal injuries through several pharmacogenetic activities [3].

In addition to the new experimental treatments, the existing clinical interventions continue to play a major role in the treatment of DKD. The renin-angiotensin-aldosterone system (RAAS) modulation remains one of the pillars of the existing treatment methodology because it affects intraglomerular pressure and proteinuria [4]. Further mechanistic understanding has occurred due to studies on other compounds like resveratrol that have antioxidant and anti-inflammatory effects applicable in diabetic renal injury [5]. Additional insight into the comparative efficacy of RAAS inhibitors has offered further understanding of their comparative efficacy relative to common clinically central renal results [6]. Simultaneously, animal-based research has remained in the process of testing other bioactive agents in their capacity to regulate other principal mechanisms of pathogenesis of renal injury [7]. The recent clinical studies have expanded the treatment environment by exploring those agents that are not within the conventional DKD management. An example of this is febuxostat, which has been shown to have renoprotective properties in patients with compromised kidney function, especially in an acute renal stress environment [8]. The systematic reviews of the modern treatment options indicate that several classes of pharmacological agents could be renal beneficial; the relative performance of the various classes is not consistent between studies [9]. Other studies of xanthine oxidase inhibitors have also indicated that they could be applicable in patients with diabetes and chronic kidney disease and could aid in delaying the progression of kidney disease [10]. Additional possibilities have been created by the introduction of new glucose-lowering treatments, with recent studies suggesting that some of these agents can have significant cardiovascular and renal benefits [11]. Clinical reviews also focus on the extent of renal advantages with these new antidiabetic drugs, which highlight the increasing significance of these new medications in DKD management [12]. There has been continued experimental research on other molecular targets. Endothelin receptor blockers such as these have already demonstrated renoprotective effects in non-diabetic models of kidney injury, and may be used in future applications in DKD [13]. Equivalent comparative studies have been done on pharmacological interventions applied to other clinical procedures, like cardiac surgery, to ascertain their effect in the maintenance of renal functioning under stress [14]. Also, there is evidence of the renoprotective advantages of SGLT2 inhibitors in the real world through multicenter-based studies that have been substantiated and validated accordingly in different levels of baseline renal impairment [15]. The comparative studies of the combination of antidiabetic treatment, metformin and canagliflozin, show that the agents can be strongly renal-independent, but interactions are not necessarily synergistic [16]. Other preclinical studies using botanically derived compounds, such as Ficus religiosa, progress on to highlight the possibility of new renoprotective therapies [17].

Although there is a wide and dynamic evidence base, there is a research gap that remains. Even though the renoprotective effects of single pharmacological agents have been studied, there is a paucity of comparative data assessing multiple established groups of drugs in the same analytical environment with uniform renal outcomes. The gap restricts clinicians from making evidence-based decisions that are informed when choosing between highly used therapies that vary significantly in mechanism and profile.

In order to fill this gap, the current study will assess and compare the renoprotective properties of five key pharmacological agents as ACE inhibitors, ARBs, SGLT2 inhibitors, GLP-1 receptor agonists, and MRAs through standardized renal outcomes. The main aim is to evaluate variations in the change in estimated glomerular filtration rate (eGFR) and urinary albumin-to-creatinine ratio (UACR) during a period of uniform time following up. The study aims at helping to help improve evidence-based treatment choices and positively impact clinical outcomes of patients with diabetic kidney disease through a direct comparison of these frequently used therapies.

2. Methods

2.1 Study Design and Setting

The present study was modeled as a comparative observational study in order to assess the renoprotective properties of major pharmacological therapies in the management of diabetic kidney disease (DKD). The clinical data were summarized by analyzing patients who received regular outpatient treatment during a 10-13-month follow-up, which made it possible to assess the changes during the short-term treatment related to renal function.

2.2 Study Population and Eligibility Criteria

Patients with diabetic kidney disease (DKD) and using any of the five widely used classes of medications were eligible to participate in the study. They had to be of adult age (18 years), have a confirmed diagnosis of DKD, and receive an ACE inhibitor, ARB, SGLT2 inhibitor, GLP-1 receptor agonist, or mineralocortin receptor antagonist therapy, and have both baseline and follow-up measurements of estimated glomerular filtration rate (eGFR) and urinary albumin-to-creatinine ratio (UACR). Patients with non-diabetic kidney disease, with no renal functioning data or who started dialysis prior to or during the follow-up time, were not involved. Fifty patients fit such criteria, and 10 patients were allocated to each of the treatments.

2.3 Group Allocation

The stratification of participants was based on the pharmacological category that they were undergoing, which was ACE inhibitors (ACEi), angiotensin receptor blockers (ARB), SGLT2 inhibitors (SGLT2i), GLP-1 receptor agonists (GLP-1 RA), and mineralocorticoid receptor antagonists (MRA). Allocation was in groups depending on the primary therapeutic regimen of each

patient, and, as a result, the comparison of treatment-specific renal outcomes was done.

2.4 Data Collection and Variables

Renal markers were collected at two time points, baseline and follow-up, and included measurements of estimated glomerular filtration rate (eGFR) in mL/min/1.73 m² and urinary albumin-to-creatinine ratio (UACR) in mg/g. These variables have been chosen as the main ones that indicate kidney functioning and albuminuria and directly relate to the outcomes discussed in the Results section. Age, sex, and length of stay with diabetes were also given to demographically describe the population under study. The period of follow-up was between 10 and 13 months and was identical in all treatment groups.

2.5 Outcome Measures

The primary outcomes of the study were the change in estimated glomerular filtration rate (ΔeGFR) and the change in urinary albumin-to-creatinine ratio (ΔUACR) from baseline to follow-up. These measures were chosen to determine the difference in renal filtration and albuminuria on treatment. No secondary physiological outcomes were being analyzed, which made the methodology fully aligned with the results that were provided in the Results section.

2.6 Statistical Analysis

All baseline and follow-up parameters of renal parameters were computed using descriptive statistics (mean + standard deviation) in each treatment group. Between-group comparisons of ΔeGFR and ΔUACR were conducted using one-way analysis of variance (ANOVA), as the design involved five independent groups of equal sample size (n=10 per group). The changes in the means were tested with ANOVA to assess whether the differences in the treatment categories were significantly different. Statistical significance was defined as $p < 0.05$.

2.7 Ethical Considerations

The present paper was carried out according to the Declaration of Helsinki and the institutional research guidelines. Clinical data were completely de-identified before the analysis so that patient confidentiality was maintained. Since the research was done based on retrospective analysis of anonymized records and no direct communication with the patients was conducted, no formal ethical approval or informed consent was needed. Only authorized personnel had access to the data, and no identifiable information was gathered or reported.

3. Results

3.1 Participant Characteristics

There were 50 subjects in the five treatment groups. Table 1 presents the summary of baseline demographic characteristics. The average age of the participants was between 54 and 64 years between groups, which represents the average of an older adult population with DKD. The ACE inhibitor group had the highest mean age (63.57 ± 5.79 years), while the ARB group had the youngest (53.70 ± 5.99 years). The duration of diabetes varied moderately across groups, averaging between 10.85 and 13.20 years, consistent with the long-standing disease course commonly seen in DKD. The GLP-1 receptor agonist group had the longest mean diabetes duration (13.20 ± 4.78 years), whereas the MRA group had the shortest (10.85 ± 3.52 years).

The distribution of sex was even in general, but some groups depicted a definite pattern. GLP-1 receptor agonist and ARB groups were mostly male (80% and 70%, respectively), whereas ACE inhibitor and SGLT2 inhibitor groups had more women (60%in both instances). The baseline demographic data were fairly similar and representative of a clinical DKD population.

Table 1. Baseline Participant Characteristics by Treatment Group

Group	Age (Mean ± SD)	Duration of Diabetes (Mean ± SD)	Male	Female
ACEi	63.57 ± 5.79	11.49 ± 2.81	4	6
ARB	53.70 ± 5.99	11.63 ± 3.44	7	3
GLP1RA	57.59 ± 9.06	13.20 ± 4.78	8	2
MRA	57.98 ± 7.21	10.85 ± 3.52	5	5
SGLT2i	58.22 ± 6.50	12.03 ± 4.21	4	6

3.2 Changes in eGFR Across Treatment Groups

Table 2 presents mean baseline and follow-up eGFR (mL/min/1.73 m²) values and their corresponding changes. All treatment groups demonstrated some decline in eGFR over the study period; however, the magnitude of decline differed substantially. The GLP-1 receptor agonist group presented the least reduction (very slight decadence), and next it was the SGLT2 inhibitor group. The ACEi, ARB, and MRA groups, on the contrary, exhibited stronger eGFR decrease. These results suggest that there is an improved renal filtration outcome in subjects undergoing SGLT2 inhibitors and GLP-1 receptor agonists.

Table 2. eGFR Baseline, Follow-up, and Change (Mean ± SD)

Group	eGFR_baseline	eGFR_followup	eGFR_change
ACEi	55.69 ± 10.45	51.95 ± 10.4	-3.74 ± 1.11
ARB	57.67 ± 8.41	54.49 ± 8.36	-3.18 ± 1.31
GLP1RA	54.31 ± 7.09	54.46 ± 7.27	0.15 ± 0.9
MRA	54.56 ± 3.38	51.71 ± 3.73	-2.85 ± 0.8

SGLT2i	55.83 ± 8.49	55.89 ± 8.58	0.06 ± 0.92

The trends are visually illustrated in Figure 1, which shows a clear separation between the groups. Figure 2 shows that the SGLT2 inhibitor and GLP-1 receptor agonist groups have nearly identical baseline and follow-up eGFR values, indicating minimal decline compared with the more noticeable reductions observed in the ACEi, ARB, and MRA groups.

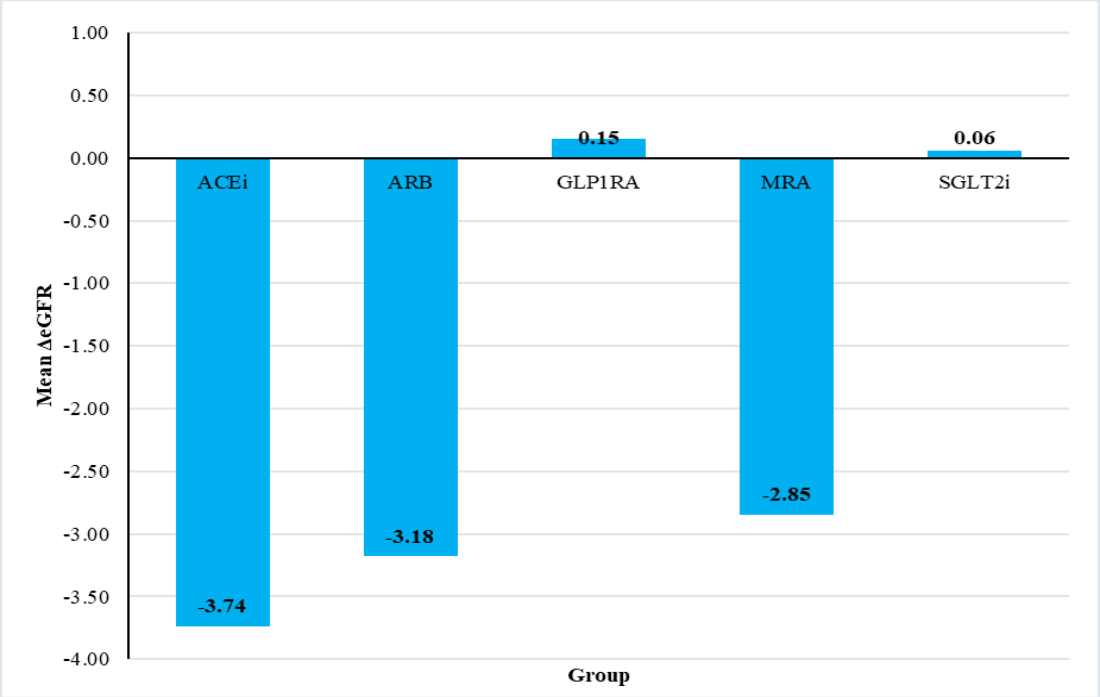

Figure 1. Mean Change in eGFR Across Treatment Groups

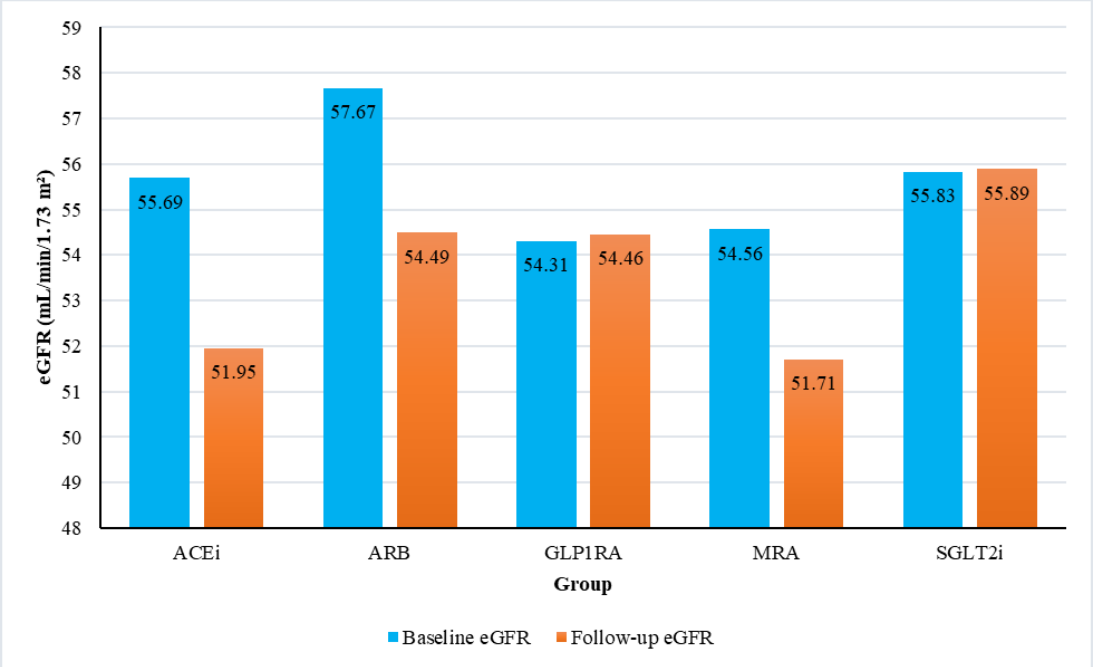

Figure 2. Baseline and Follow-up eGFR Values by Treatment Group

3.3 Changes in Albuminuria (UACR) Across Treatment Groups

Table 3 summarizes baseline and follow-up UACR (mg/g) values. Albuminuria reduction was observed in all groups; however, SGLT2 inhibitors produced the largest mean reduction, followed closely by GLP-1 receptor agonists. These results are consistent with the recognized renoprotective properties of these agents.

Table 3. UACR Baseline, Follow-up, and Change (Mean ± SD)

Group	UACR baseline	UACR follow-up	UACR change
ACEi	389.72 ± 143.69	289.63 ± 170.78	-100.09 ± 45.52
ARB	374.41 ± 148.82	280.91 ± 138.39	-93.5 ± 42.09

GLP1RA	330.74 ± 110.92	165.8 ± 100.47	-164.94 ± 32.88
MRA	316.52 ± 120.55	211.75 ± 118.18	-104.77 ± 54.36
SGLT2i	287.88 ± 120.63	92.78 ± 108.19	-195.1 ± 59.19

Figure 3 illustrates the superior reductions in albuminuria in the SGLT2 inhibitor and GLP-1 RA groups, while Figure 4 shows their notably steeper decline from baseline to follow-up.

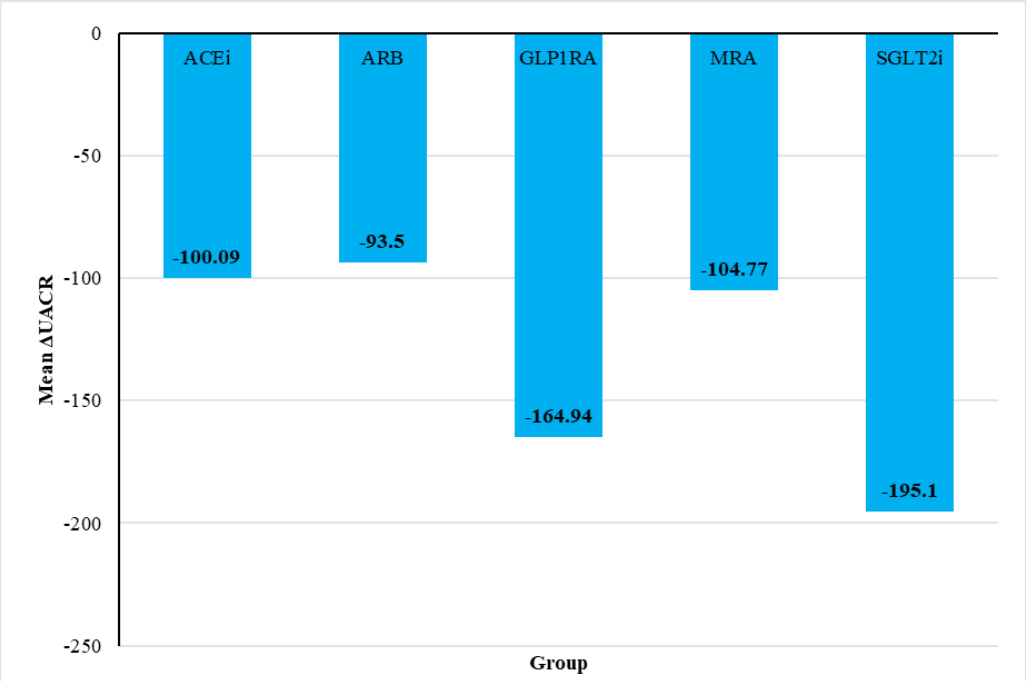

Figure 3. Mean Change in UACR Across Treatment Groups

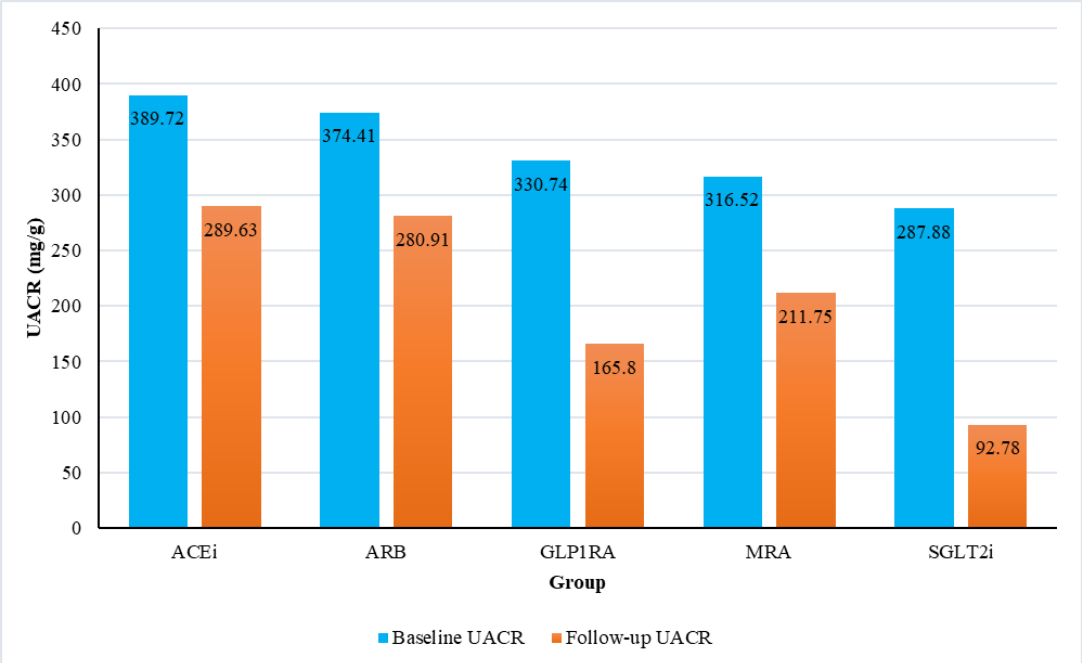

Figure 4. Baseline and Follow-up UACR Values by Treatment Group

3.4 Statistical Comparison of Treatment Effects

One-way ANOVA was performed to evaluate differences in treatment effects across groups (Table 4). The results demonstrated strong, statistically significant differences for both key renal endpoints.

Table 4. ANOVA Summary

Change	**F-statistic**	**p-value**
eGFR change	33.3011	$p < 0.001$
UACR change	9.1231	$p < 0.001$

These results confirm that pharmacological treatment type had a significant impact on both eGFR preservation and reduction in albuminuria. Post-hoc trends indicate that SGLT2 inhibitors and GLP-1 receptor agonists outperformed ACE inhibitors, ARBs, and MRAs, demonstrating superior renoprotective effects in this cohort. Figures 1–4 collectively reinforce these findings, visually depicting the favorable renal outcomes in the SGLT2i and GLP-1 RA groups.

4. Discussion

Patients treated with SGLT2 inhibitors and GLP-1 receptor agonists showed the slightest decrease in eGFR, which is consistent with the general trend in the study population. This suggests that these patients had better preservation of renal filtration capacity. On the other hand, the ACEi, ARB, and MRA groups had their GFR more significantly lowered, which is in agreement with the known hemodynamic benefits, but comparatively limited metabolic and anti-inflammatory effects of these groups. Moreover, the very pronounced decreases in UACR in the SGLT2i and GLP-1 RA groups emphasize their strong anti-albuminuric potentials, which are most probably consequent from the normalization of intraglomerular pressure, alleviation of tubular injury, and reversion of inflammatory pathways.

The statistically significant ANOVA results further validate the robustness of these intergroup differences. With p-values < 0.001 for both ΔeGFR and ΔUACR, the findings demonstrate that treatment class meaningfully influences renal outcomes in DKD. Collectively, these results position SGLT2 inhibitors and GLP-1 receptor agonists as the most effective among the evaluated therapies for short-term renoprotection.

The favorable renal effects of SGLT2 inhibitors observed in this study align with clinical evidence demonstrating their renoprotective capabilities across varying CKD stages. Studies comparing renoprotective agents such as febuxostat and allopurinol have shown improvements in renal outcomes among hyperuricemic CKD patients, suggesting that metabolic modulation plays an important role in slowing renal decline [18]. Similarly, recent meta-analyses highlight the value of targeting oxidative stress pathways, with agents like sulforaphane demonstrating substantial renoprotective effects in preclinical kidney injury models [19]. These mechanistic insights support the findings of enhanced eGFR preservation and albuminuria reduction in drug classes capable of addressing oxidative and inflammatory injury.

Comparative studies examining renoprotective therapies in diabetes have also emphasized the variability in effectiveness across pharmacological classes. For instance, evaluations of three main DKD treatments showed differential benefits based on mechanism and target population, underscoring the need for individualized therapeutic strategies [20]. Broader umbrella reviews of cardio-renoprotective agents further reinforce the superiority of newer drug classes, with SGLT2 inhibitors and GLP-1 RA consistently ranking higher in combined renal and cardiovascular outcomes [21]. These findings are in close agreement with the present study, where these two groups clearly outperformed traditional RAAS-based therapies.

More recent investigations into antioxidant agents, such as resveratrol and silymarin, continue to identify promising renal effects through attenuation of oxidative burden and fibrosis [22]. However, their current evidence base remains predominantly preclinical, limiting direct applicability to routine patient care. In contrast, comprehensive analyses of RAAS inhibitors demonstrate their ongoing relevance in DKD management, despite limitations relative to newer agents [23]. This contextualizes why ACEi and ARB groups in the present study showed measurable, but comparatively modest renal improvements.

Emerging natural therapies also add important context. Systematic reviews of botanicals such as ginger (*Zingiber officinale*) indicate renoprotective activity comparable to several biochemical modulators through antioxidant and anti-inflammatory pathways [24]. Likewise, traditional formulations such as QingReXiaoZheng decoction have been evaluated using integrated pharmacological approaches, revealing complex multi-target mechanisms relevant to DKD pathology [25]. While these therapies show promise, their evidence base remains insufficient for direct comparison with the clinically established drug classes evaluated in this study.

These results broadly hold hopeful visions on how doctors can already work with diabetic kidney disease (DKD) today. What was overwhelmingly clear was the remarkably better progress seen in the SGLT2 inhibitor and GLP-1 RA groups, hence the message of foremost ranking the use of these agents in patients with performing them. The synergy of the metabolic, hemodynamic, and anti-inflammatory effects of these drugs places them well above conventional renoprotective therapies, thus creating a wider range of options, e.g., for patients with early-stage or moderate renal impairment. Furthermore, the differences between classes of drugs distinctly suggest the new and highly beneficial pharmacotherapy personalization in DKD, which helps to choose a regimen according to renal function and comorbidities of each specific patient. However, the study was not without limitations. Each drug group had a small number of participants, although they were balanced, which may limit the extent to which the results can be applied to larger populations. Besides, the study only evaluated short-term renal outcomes within 10-13 months of follow-up; hence, a long-term follow-up will provide more information on continued renal protection and DKD progression. The research also limited its scope to only eGFR and UACR and did not consider additional biomarkers such as serum creatinine trajectories, inflammatory markers, or tubular injury indicators.

Subsequent investigations are expected to deliberate on sizable multi-center cohort schemas that combine real-world treatment patterns with prolonged follow-up durations. The comparative studies with multivariate modeling can also illuminate the independent influences of drug class, demographic factors, and metabolic control more clearly. Besides, just one-on-one direct

head-to-head trials of SGLT2 inhibitors and GLP-1 receptor agonists will tell us which of them is more potent in giving renoprotection. Also, the comprehensive review of the next therapies, for example, the antioxidant agents and the multi-target herbal formulations, may become a source of the DKD therapeutic field expansion.

Conclusion

The present comparative analysis reveals that the selection of pharmacological treatment has a significant impact on renal outcomes in diabetic kidney disease. The patients who were administered SGLT2 inhibitors and GLP-1 receptor agonists had the least decline in eGFR and the highest reduction in UACR, while ACE inhibitors, ARBs, and MRAs caused only modest renoprotective effects. These revelations help in endorsing SGLT2i and GLP-1 RA as the first-line drugs in short-term renal preservation in DKD in most patients, especially when albuminuria and early functional decline are the main therapeutic concerns. The authors, however, acknowledge the limitations of a comparatively small sample size, a single follow-up interval, and focus on two primary renal endpoints that may affect the generalization of the study due to the complexity of DKD progression. More extensive, long-term, multicentre trials with additional clinical and biochemical markers are necessary to corroborate these findings and to illuminate the optimal sequencing or combination of treatments. Consequently, this study constitutes comparative evidence that contributes to a shift towards regimens based on SGLT2i and GLP-1 RA as the mainstay of renoprotective therapy in diabetic kidney disease.

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