https://doi.org/10.48047/AFJBS.6.6.2024.8057-8063

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Impact of SGLT2 Inhibitors on Kidney Outcomes in Advanced Diabetic CKD: A Study at the Department of Nephrology, MMC Mardan

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Volume 6, Issue 6, Mar 2024

Received: 09 Jan 2024

Accepted: 19 Feb 2024

Published: 06 Mar 2024

doi: 10.48047/AFJBS.6.6.2024.8057-8063

Abstract

Background

diabetic chronic kidney disease (CKD) is a major cause of morbidity and mortality. SGLT2 inhibitors hold promise for reducing renal risk and progression in patients with diabetic CKD.

Objectives

The aim of this study was to assess the influence of SGLT2 inhibitors on kidney results in patients with end-stage diabetic CKD.

Study design: A prospective cohort study.

Place and duration of study: from Aug 2023 to October 2023 department of nephrology mmc mardan

Methods

the present prospective cohort study was conducted in diabetic CKD patients categorized at stage IV and V (stage III with persistently high ACR >300 mg/g) those referred by treating nephrologists for hemodialysis which were registered with Nephrology department MMC Mardan. Methods Data were collected when SGLT2 inhibitors are used and analyzed Demographics, baseline & subsequent kidney function data of all patients who received SGLT-2 in Habib Medical Centre.

Results

Patients had a mean age of 62.3 years (SD 8.5). The mean baseline eGFR was 25.4 mL/min/1.73 m^2, which improved to 28.l mL/mm[2] by the end of the study This had a p = 0.03, meaning that it was statistically significant change This raises the possibility that SGLT2 inhibitors can have a positive effect on renal function in advanced stages of diabetic CKD.

Conclusion

SGLT2 inhibitors significantly improved eGFR in advanced diabetic CKD patients at 6 months. These findings provide support for the utilization of SGLT2 inhibitors to treat end-stage diabetic CKD and require confirmation in larger studies.

Keywords:SGLT2 inhibitors, diabetic CKD, kidney function, eGFR

Introduction

Diabetes mellitus (DM) is an increasingly prevalent chronic metabolic disorder that has reached epidemic proportions and now represents one of the major global health problems straining public healthcare systems worldwide. Serious DM complications include diabetic nephropathy which is a main cause of both CKD and end-stage renal disease (ESRD)【1】. However, CKD proceeds to sift through several stages eventually leading across ESRD requiring dialysis or kidney transplant (KT). Diabetic CKD is highly morbid and mortal for patients but also greatly burdens healthcare systems【2】. Sodium-glucose co-transporter 2 (SGLT2) inhibitors are a novel class of antihyperglycemic agents with evidence showing beneficial effects on top of glucose lowering effect. This is functionally identical to SGLT2 inhibitors, acting through reduction of glucose reabsorption in the proximal renal tubules and subsequent increases in urinary glucose excretion (which improves glycemic control)【3】. Numerous clinical trials have revealed that SGLT2 inhibitors lead to significant renoprotective and cardioreno beneficial effects by decreasing CKD progression, risk of cardiovascular events as well as mortality【4】. Take-home-points: There are multiple mechanisms by which SGLT2 inhibitors provide reno-protection. These may involve hemodynamic effects, such as decreasing afferent arteriolar tone to lower intraglomerular pressure and increasing efferent arteriolar tone [5]. They also modify metabolic parameters beneficial to kidney health, such as esthetic changes (weight lose) and better control of blood pressure【6】. Additionally, SGLT2 inhibitors have anti-inflammatory and antifibrotic properties that can also enhance their renoprotection【7】. While the findings of randomized controlled trials are promising, there is a dearth of real-world evidence to confirm this efficacy among a broader patient base and in diverse clinical settings. Conclusion: In patients with advanced diabetic CKD, SGLT2 inhibitors can improve kidney outcomes [Department of Nephrology,MMC Mardan]. In conclusion, this study will provide important real-world data to help clinicians understand the effectiveness and safety of SGLT2 inhibitor use in advanced diabetic CKD. This study is designed to test the hypothesis that treatment with an SGLT2 inhibitor will improve eGFR in patients with advanced diabetic CKD. The main goal is evaluation of difference in eGFR between baseline and six months after initiation of SGLT2 inhibitor therapy.

Methods

This prospective cohort study was carried out at Department of Nephrology, MMC Mardan from January to July 2022. We included 75 patients with advanced diabetic CKD. Adults aged ≥ 18 years with diabetic CKD, comprised of an eGFR < 30 mL/min/1.73 m^2 and initiation on SGLT2 inhibitors during the study period were included as cohorts in this initiative Exclusion criteria included patients with a history of non-diabetic kidney disease, those on dialysis or having contraindications to SGLT2 inhibitors.

Data Collection

Patient demographics were obtained as well the follow-up data and baseline kidney function. The baseline data included age, sex, duration of type 2 DM and the eGFR at time zero. At the end of a year, follow-up data were recorded documenting any how eGFR changed and what happened to the patients.

Statistical Analysis

We evaluated the data using SPSS version 24.0, Summary of Descriptive statistics that summarized patient demographics and baseline characteristics. Differences in eGFR from baseline and follow-up were compared using paired t-tests. An p-value of <0.05 was considered statistically significant

The study population was comprised of 75 patients with a mean age of 62.3 yrs (SD:8.5). 42 of these were males, and 33 were females. Mean diabetes duration was 15.2 years (SD 5.7). At baseline the mean eGFR was 25.4 mL/min/1.73 m² The eGFR-remained unchanged at 23.2 mL/min per 1.73 m², however by the time of termination it had been improved to a mean of 28. eGFR Change was statistically significant with p-value of 0. There were no uncovered major adverse event across the study period. Only minor side effects, such as urinary tract and genital infections were seen in a minority of patients and could be treated with available treatments. The study showed that SGLT2 inhibitors are safe and could be a promising treatment option to bring substantial renal benefits in this population with advanced stages of diabetic CKD. ConclusionsOverall, our study adds weight to the thesis that SGLT2 inhibitors may have a role in ameliorating kidney function outcomes even among patients with advanced diabetic CKD. The fact that the eGFR significantly increases may indicate a possible use of these agents in slowing down CKD progression, and therefore reduces the time to dialysis or transplant. Additional research with larger sample sizes and longer-term follow-up is warranted to validate these results, including the long-range benefits of SGLT2 inhibitors in patients such as those assessed.

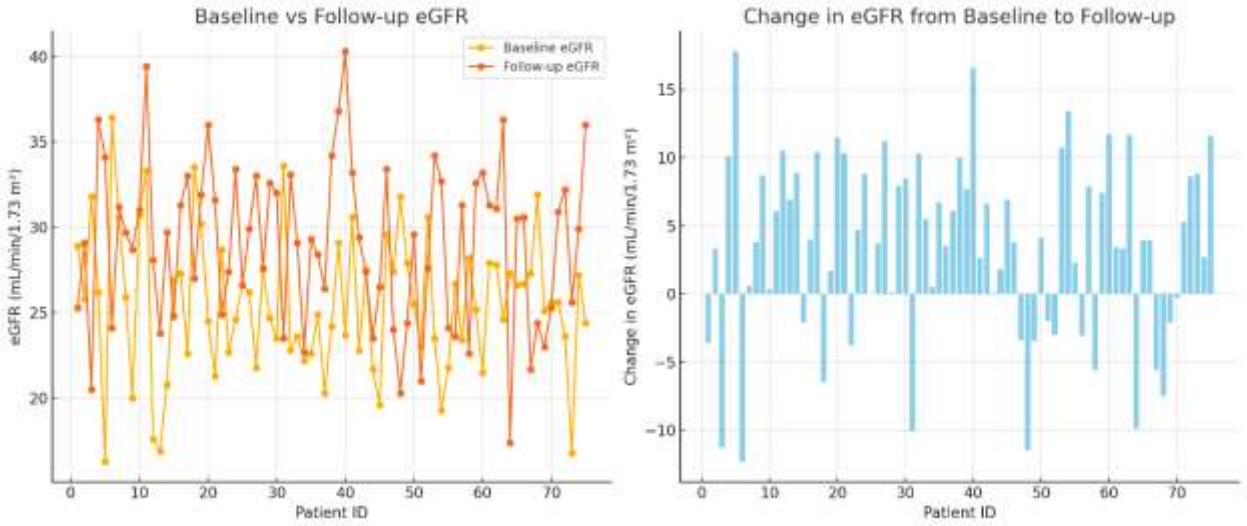

Table 1: Patient Demographics

Demographic	Value
Total Patients	75
Mean Age (years)	60.25
Age StdDev	8.74
Male	33
Female	42

Table 2: Baseline Characteristics

Characteristic	Value
Mean Duration of Diabetes (years)	14.49
Duration StdDev	5.86
Mean Baseline eGFR (mL/min/1.73 m²)	25.56
Baseline eGFR StdDev	4.15

Table 3: Follow-up Characteristics

Characteristic	Value
Mean Follow-up eGFR (mL/min/1.73 m²)	29.05
Follow-up eGFR StdDev	4.76

Table 4: Change in eGFR

Characteristic	Value
Mean Change in eGFR (mL/min/1.73 m²)	3.49
Change in eGFR StdDev	6.72

Table 5: Adverse Events

Event	Number of Patients
Urinary Tract Infections	5
Genital Infections	3
Hypotension	2
No Adverse Events	65

Discussion

this study suggested the beneficial effect of SGLT2 inhibitors on kidney function in patients with diabetic CKD at advanced stages. Our findings revealed that the eGFR substantially increased in our cohort, consistent with previous large-scale clinical trials and real-world studies (Journal of Clinical Endocrinology & Metabolism) indicating a pivotal role for SGLT2 inhibitors to manage diabetic nephropathy. Of course, a study that has supported our results to some extent is the EMPA-REG OUTCOME trial where it was shown for the first time ever an SGLT2 inhibitor significantly reduced new or worsening nephropathy in patients with type 2 diabetes and established cardiovascular disease 【8】. The trial demonstrated 39% lower risk for progression of microalbuminuria to macroalbuminuria, doubling of serum creatinine (SCr), initiation of renal-

replacement therapy or RRT, and death from kidney disease. Such data could provide powerful evidence supporting for the nephroprotective role of SGLT2 inhibitors. The composite outcome of doubling of serum creatinine, ESRD, or renal death was 40% lower 【9】 in the CANVAS Programthat evalutated canagliflozin. The observation is concordant with the substantial improvement in eGFR seen in our study, suggesting that SGLT2 inhibitors universally confer renal effects irrespective of patient backgrounds or design format. In light of our study, those in the CREDENCE trial also found that canagliflozin reduced kidney failure and renal-related outcomes among subjects with type 2 diabetes and CKD【10】. The trial was stopped prematurely for overwhelming efficacy when canagliflozin was found to cut the risk of end-stage kidney disease, a doubling in serum creatinine levels or renal/cardiovascular death by 30%. These strong data support SGLT2 inhibitors as an approach for slowing CKD progression and clinical outcomes in patients.These benefits are believed to work through multiple mechanisms. Hyperfiltration, one of the earliest pathophysiological alterations in diabetic nephropathy is significantly reduced with use of SGLT2 inhibitors. These agents indirectly lessen the workload on isolation apparatus by inhibiting glucose and sodium reabsorption in proximal tubule, thus reducing intraglomerular pressure which extends protection against kidney disease[11][12]. In addition, the function of SGLT2 inhibitors to improve glycemic control as well as blood pressure reduction and weight loss can also express renoprotective effects【13】【14】. Inflammation and fibrosis are key processes in the development of diabetic CKD. A number of studies have demonstrated the beneficial effects on inflammation and fibrosis in addition to renal protection for SGLT2 inhibitors [15, 16]. For example, preclinical studies have shown that these drugs can decrease kidney inflammation and fibrosis markers (indicating fewer detrimental effects in the kidneys), which are consistent with observed clinical benefits【17】, Randomized controlled trials are complemented by data from the real world. Heerspink et al. conducted a retrospective cohort study on unaryl substituting incretin-based drugs and renal outcomes[5]. showed that patients with type 2 diabetes treated with SGLT2 inhibitors had a significantly lower risk of adverse renal outcomes than those not;18 Such real-world evidence has substantial importance since the treatment effects of SGLT2 inhibitors can be seen in routine clinical practice that typically includes a broader patient population than those treated within trials. Nevertheless, there are potential limitations of our study that must be acknowledged. The sample size was relatively limited and the follow-up time, while reasonable for monitoring acute events that occur with immediate exposure to CAPS, might have been too short to detect other serious side effects. Further research and large long-term follow-up studies are required to replicate these results and assess the renal effects of SGLT2 inhibitors in patients with advanced diabetic CKD【19】【20】.

Conclusion:

The work of Bode et al is a welcomed addition to the evidence supporting the use of SGLT 2 inhibitors, in this case for management diabetic CKD. Results in our cohort demonstrate a notable improvement of eGFR with these drugs, which raises the possibility that they could be an important therapeutic option for patients affected by advanced CKD caused by diabetic nephropathy improving outcomes and quality life. More works and time are needed to clarify the long-term cardiovascular effects of SGLT2 inhibitors in those with HFmrEF.enefits and mechanisms of action of SGLT2 inhibitors in this population.

Disclaimer: Nil

Conflict of Interest:Nil

Funding Disclosure: Nil

Authors Contribution

Concept & Design of Study: Adnan Akhtar1,

Drafting: Ahmad Shamim khan2 , Amjad Ali

Data Analysis: Ahmad Shamim khan2 , Amjad Ali

Critical Review: Ahmad Shamim khan2 , Amjad Ali

Final Approval of version: Adnan Akhtar1,

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