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Short Communication

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RENOPROTECTIVE EFFECTS OF SODIUM GLUCOSE COTRANSPORTER-2 INHIBITORS IN TYPE 2 DIABETES MELLITUS: MECHANISTIC INSIGHTS, CLINICAL EVIDENCE, AND THERAPEUTIC IMPLICATIONS

Syed Afzal Uddin Biyabani[1]*, Zunera Fatima[1], Pooja V. Salimath[1], Vanishree P. Babladi[1], Hafsa Naema[2], Safa Wasay[3]

[1]Research Scholar, Department of Pharmacy Practice, Rajiv Gandhi University of Health Sciences, Kalaburagi, Karnataka, India.

[1]PharmD Graduate, Dept. of Pharmacy Practice, Deccan School of Pharmacy, Hyderabad, Telangana, India.

[1]Associate Professor and Research Scholar, Dept. of Pharmacy Practice, Matoshree Taradevi Rampure Institute of Pharmaceutical Sciences, Kalaburagi, Karnataka, India.

[1]Assistant Professor, Department of Pharmacy Practice, Matoshree Taradevi Institute of Pharmaceutical Sciences, Kalaburagi, Karnataka, India.

[2]PharmD Graduate, Dept. of Pharmacy Practice, Matoshree Taradevi Rampure Institute of Pharmaceutical Sciences, Kalaburagi, Karnataka, India.

[3]PharmD Scholar, Dept. of Pharmacy Practice, Jawaharlal Nehru Technological University, Hyderabad, Telangana, India.

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***Corresponding Author: Syed Afzal Uddin Biyabani**

Research Scholar, Department of Pharmacy Practice, Rajiv Gandhi University of Health Sciences, Kalaburagi, Karnataka, India.

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ABSTRACT

Background: Diabetic kidney disease (DKD) is a major microvascular complication of type 2 diabetes mellitus (T2DM) and represents one of the leading causes of chronic kidney disease and end-stage renal failure globally. Conventional therapies often slow but do not prevent progressive renal decline. Recently, sodium–glucose cotransporter-2 (SGLT2) inhibitors have emerged as a novel therapeutic class demonstrating significant renal protective effects beyond glycaemic control.**Objective:** To highlight emerging mechanistic insights and clinical evidence supporting the renoprotective benefits of SGLT2 inhibitors in

patients with T2DM. **Observation:** Clinical studies and real-world evidence indicate that SGLT2 inhibitor therapy is associated with reductions in albuminuria, stabilization of estimated glomerular filtration rate (eGFR), and decreased risk of progression to end-stage renal disease. **Conclusion:** SGLT2 inhibitors represent a paradigm shift in diabetes management by offering both metabolic and renal protection. Their incorporation into clinical practice may significantly reduce the burden of diabetic kidney disease.

KEYWORDS: SGLT2 inhibitors, diabetic nephropathy, renal protection, type 2 diabetes mellitus, chronic kidney disease.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) has become one of the most prevalent non-communicable diseases worldwide and is associated with substantial morbidity and mortality. According to global epidemiological estimates, the prevalence of diabetes continues to rise due to increasing obesity rates, sedentary lifestyle patterns, and population aging[1]. Among the numerous complications associated with T2DM, diabetic kidney disease (DKD) represents a particularly serious concern because it significantly increases the risk of cardiovascular events, hospitalization, and premature death[2].

DKD affects approximately one-third of individuals with diabetes and remains the most common cause of end-stage renal disease requiring dialysis or kidney transplantation in many regions of the world[3]. The pathogenesis of diabetic nephropathy is multifactorial and involves chronic hyperglycaemia-induced metabolic disturbances, hemodynamic changes, oxidative stress, and inflammatory pathways that progressively damage renal structures[4].

Persistent hyperglycaemia leads to the formation of advanced glycation end products and activation of protein kinase C pathways, which contribute to glomerular hypertrophy, mesangial expansion, and thickening of the glomerular basement membrane. These structural changes ultimately lead to progressive loss of renal filtration capacity and increased urinary albumin excretion[5].

Traditional therapeutic approaches for diabetic kidney disease have focused primarily on strict glycaemic control, blood pressure management, and inhibition of the renin–angiotensin–aldosterone system using angiotensin-converting enzyme inhibitors or angiotensin receptor blockers[6]. While these strategies have improved clinical outcomes, they do not completely prevent disease progression in many patients.

Recent advances in pharmacotherapy have introduced sodium–glucose cotransporter-2 (SGLT2) inhibitors, a novel class of oral antidiabetic medications that have demonstrated significant renal and cardiovascular benefits. These agents reduce renal glucose reabsorption by inhibiting the SGLT2 transporter located in the proximal renal tubules, thereby promoting glycosuria and improving glycaemic control[7].

Importantly, emerging evidence indicates that the benefits of SGLT2 inhibitors extend beyond glucose lowering and include substantial renoprotective effects, which may significantly alter the natural history of diabetic kidney disease.

CLINICAL OBSERVATION AND EMERGING EVIDENCE

In routine clinical practice, patients with T2DM treated with SGLT2 inhibitors such as empagliflozin, dapagliflozin, and canagliflozin frequently demonstrate improvements in renal function parameters. Several observational studies have reported reductions in urinary albumin-to-creatinine ratio and slower decline in estimated glomerular filtration rate.

These benefits appear to occur relatively early during therapy and may persist over long-term treatment. Furthermore, large randomized clinical trials have shown that SGLT2 inhibitor therapy significantly reduces the risk of renal endpoints including sustained decline in eGFR, progression to end-stage renal disease, and requirement for renal replacement therapy.

MECHANISMS OF RENAL PROTECTION

The renoprotective effects of SGLT2 inhibitors are mediated through several complementary physiological mechanisms.

Restoration of Tubuloglomerular Feedback

In diabetes, increased glucose and sodium reabsorption in the proximal tubule reduces sodium delivery to the macula densa, resulting in afferent arteriolar dilation and increased intraglomerular pressure. This phenomenon contributes to glomerular hyperfiltration and progressive kidney damage. SGLT2 inhibitors restore tubuloglomerular feedback by increasing sodium delivery to the macula densa, thereby reducing intraglomerular pressure and improving renal hemodynamic[8].

Reduction of Renal Inflammation and Fibrosis

Experimental studies suggest that SGLT2 inhibitors reduce inflammatory cytokine production and inhibit fibrotic pathways that contribute to chronic kidney injury. These anti-

inflammatory effects may play an important role in slowing the progression of diabetic nephropathy[9].

Metabolic and Hemodynamic Benefits

SGLT2 inhibitors also provide several systemic benefits including modest weight loss, reduction in blood pressure, and improved metabolic control. These effects indirectly contribute to improved renal outcomes and reduced cardiovascular risk.

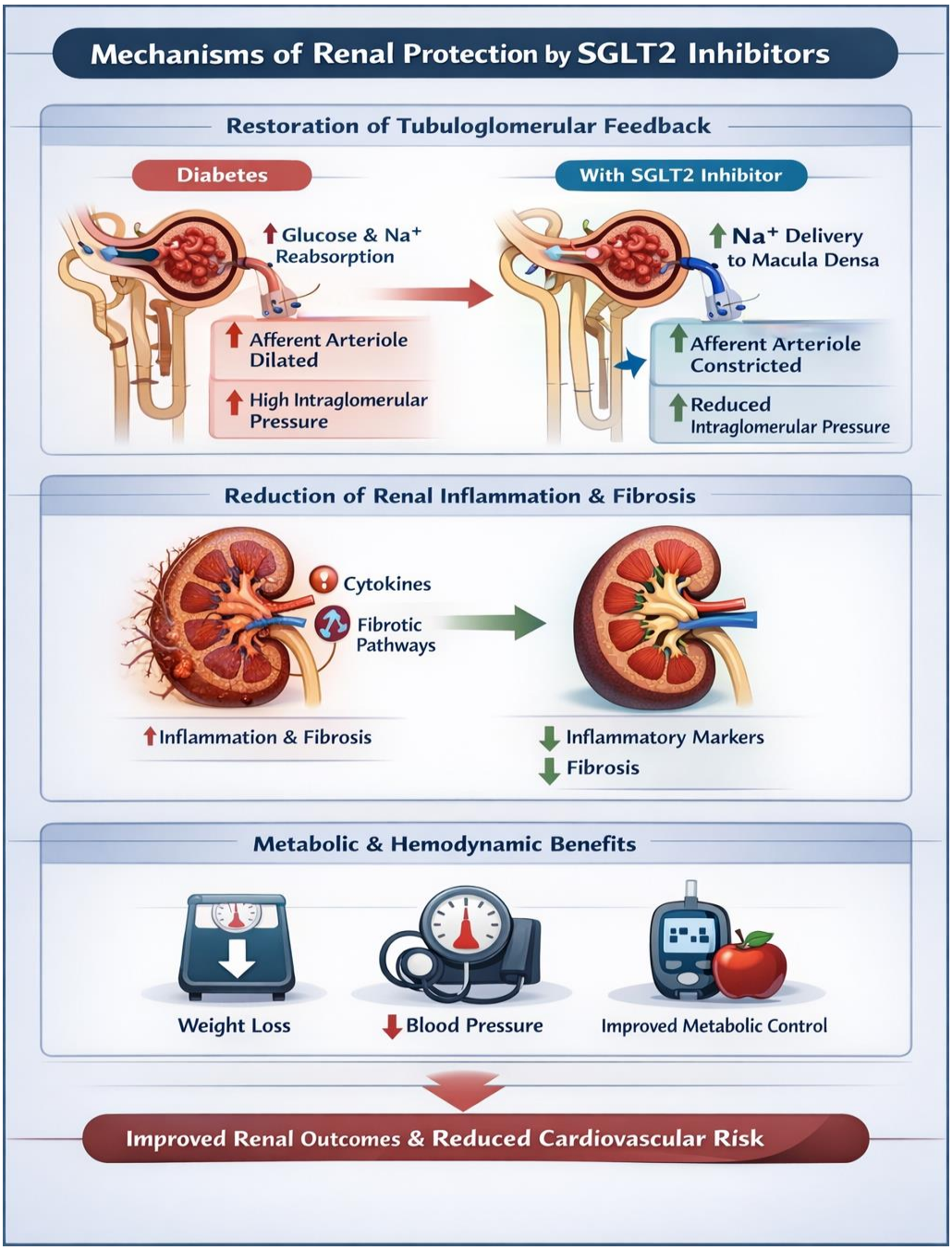

Figure 1: Mechanisms of Renal Protection by SGLT2 Inhibitors Integrated Effects on Tubuloglomerular Feedback, Inflammation, Fibrosis, and Metabolic Hemodynamic.

DISCUSSION

The introduction of SGLT2 inhibitors has significantly transformed the therapeutic landscape of type 2 diabetes mellitus. Several landmark clinical trials have provided strong evidence supporting the renal protective benefits of these agents.

The EMPA-REG OUTCOME trial demonstrated that empagliflozin significantly reduced the risk of progression of kidney disease and renal failure among patients with T2DM and established cardiovascular disease[10]. Similarly, the CREDENCE trial reported that canagliflozin significantly reduced the risk of kidney failure and cardiovascular events in patients with diabetic nephropathy[11].

Another important study, the DAPA-CKD trial, demonstrated that dapagliflozin reduced the risk of worsening kidney function and mortality in patients with chronic kidney disease, even among those without diabetes[12]. These findings suggest that the renoprotective effects of SGLT2 inhibitors may extend beyond their glucose-lowering properties.

Despite these benefits, certain safety considerations must also be acknowledged. SGLT2 inhibitors have been associated with adverse effects such as genital infections, volume depletion, and rare cases of euglycemic diabetic ketoacidosis. Appropriate patient selection and clinical monitoring are therefore essential to ensure safe use of these medications.

CLINICAL PRACTICE IMPLICATIONS

The accumulating evidence supporting the renal benefits of SGLT2 inhibitors has led to their increasing incorporation into international diabetes management guidelines. Current recommendations emphasize their use in patients with T2DM who have chronic kidney disease or high cardiovascular risk.

By slowing the progression of diabetic nephropathy and reducing the risk of renal failure, SGLT2 inhibitors have the potential to substantially reduce healthcare burden and improve long-term outcomes in patients with diabetes.

FUTURE PERSPECTIVES

Future research should focus on further elucidating the molecular mechanisms underlying the renoprotective effects of SGLT2 inhibitors. Long-term observational studies are also needed to better understand their impact on kidney disease progression and survival outcomes in diverse patient populations.

CONCLUSION

SGLT2 inhibitors represent a major therapeutic advancement in the management of type 2 diabetes mellitus. Their ability to provide significant renal protection in addition to glycaemic control highlights their importance in modern diabetes therapy. Continued clinical research and pharmacovigilance will be essential to optimize their use and maximize patient benefit.

REFERENCES

1. International Diabetes Federation. *IDF Diabetes Atlas*. 10th ed. Brussels: International Diabetes Federation; 2021
2. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: results from the International Diabetes Federation Diabetes Atlas. *Diabetes Res Clin Pract* 2019; 157:107843
3. American Diabetes Association. Standards of medical care in diabetes—2024. *Diabetes Care* 2024;47(Suppl 1): S1–S350
4. DeFronzo RA, Ferrannini E, Groop L, Henry RR, Herman WH, Holst JJ, et al. Type 2 diabetes mellitus. *Nat Rev Dis Primers* 2015; 1:15019
5. Forbes JM, Cooper ME. Mechanisms of diabetic complications. *Physiol Rev* 2013;93(1):137–88
6. Brenner BM, Cooper ME, de Zeeuw D, Keane WF, Mitch WE, Parving HH, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med* 2001;345(12):861–69
7. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med* 2015;373(22):2117–128
8. Heerspink HJL, Stefansson BV, Correa-Rotter R, Chertow GM, Greene T, Hou FF, et al. Dapagliflozin in patients with chronic kidney disease. *N Engl J Med* 2020;383(15):1436–46
9. Perkovic V, Jardine MJ, Neal B, Bompoint S, Heerspink HJL, Charytan DM, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. *N Engl J Med* 2019;380(24):2295–306
10. Neal B, Perkovic V, Mahaffey KW, de Zeeuw D, Fulcher G, Erondu N, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. *N Engl J Med* 2017;377(7):644–57

11. Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. *N Engl J Med* 2019;380(4):347–57
12. Packer M, Anker SD, Butler J, Filippatos G, Pocock SJ, Carson P, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. *N Engl J Med* 2020;383(15):1413–24