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RESEARCH ARTICLE

REVIEW OF EVALUATING THE EFFICACY AND SAFETY OF SITAGLIPTIN VS DAPAGLIFLOZIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND RENAL IMPAIRMENT

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Abstract: Type 2 diabetes mellitus and kidney disease are interlinked, with the coexistence of these conditions complicating therapeutic decisions, especially concerning antidiabetic agents. This review critically examines the efficacy and safety profiles of sitagliptin and dapagliflozin in managing T2DM in patients with renal impairment. Drawing from clinical trials and population studies, dapagliflozin appears superior in reducing cardiovascular and renal outcomes but poses a higher risk of genital infections, while sitagliptin shows favorable glycemic control with minimal risk of hypoglycemia but may be associated with a higher risk of acute kidney injury. Additional focus is placed on drug mechanisms, dosing adjustments, and their applicability in different stages of renal dysfunction. Dapagliflozin has demonstrated strong renal and cardiovascular protective effects, making it a preferred option in patients at high risk of complications, whereas sitagliptin remains a valuable alternative in elderly patients or those with mild renal impairment due to its better safety and tolerability. Both agents need to be considered individually as per renal status, comorbidity, and patient-related issues. Highlighting a personalized, evidence-based approach, this review outlines the clinical relevance of these therapies and their broader implications for managing diabetic kidney disease.

Keywords: Type 2 diabetes mellitus, Renal Impairment, Sitagliptin, Dapagliflozin, Hyperkalemia, Antidiabetic Agents.

INTRODUCTION

Type 2 Diabetes Mellitus is a global cause of morbidity and mortality, and chronic kidney disease is one of the most severe long-term complications. Both conditions independently increase the risk of cardiovascular events, and their coexistence exacerbates clinical outcomes and healthcare costs[9]. Hyperglycemia accelerates renal damage, while impaired kidney function limits the therapeutic options for glycemic control. Traditional antidiabetic agents such as metformin require caution or are contraindicated in renal impairment. Newer drug classes such as SGLT2 inhibitors and DPP-4 inhibitors have emerged with varying degrees of efficacy and safety in this population. A number of large-scale trials and meta-analysis have shown that SGLT2 inhibitors such as dapagliflozin not only enhance glycemic control but also retard CKD progression and lower hospitalization due to heart failure [2] [4]. DPP-4 inhibitors like sitagliptin offer a well-tolerated alternative, especially in patients who are elderly or have multiple comorbidities[5]. This review synthesizes current research comparing these two agents to guide clinical decision-making.

DEFINITION AND PREVALENCE

T2DM is a metabolism disorder characterized by chronic hyperglycemia resulting from insulin resistance and relative insulin deficiency. Chronic Kidney Disease is defined as a decline in renal function, indicated by a glomerular filtration rate (GFR) less than 60 mL/min/1.73m^2 or evidence of kidney damage persisiting for more than three months. Almost 30-40% of patients with T2DM will develop some degree of CKD throughout their disease [9]. Based on population-based research, the combination of diabetes and CKD is correlated with an exceedingly higher risk of cardiovascular disease, hospitalization, and all-cause mortality[2]. Causes of the widespread prevalence include aging population, rising levels of obesity, hypertension, and physical inactivity. Early detection, routine screening, and quick help can significantly decrease complications and improve the standard of living. Healthcare systems all over the world are increasingly taking a combined strategy to address the double burden of diabetes and renal disease.

PATHOPHYSIOLOGY

The pathophysiology of T2DM with renal damage is a multifactorial process. Chronic hyperglycemia results in non-enzymatic protein glycation, oxidative stress, and

activation of inflammatory pathways that lead to structural and functional alterations in the kidneys. These are glomerular hyperfiltration, increased thickness of the glomerular basement membrane, and mesangial expansion(Fig. 1). These changes ultimately lead to a reduction in glomerular filtration rate (GFR), eventually resulting in chronic kidney disease (CKD). SGLT2 inhibitors such as dapagliflozin act by lowering glucose and sodium reabsorption in the renal tubules proximal to the glomerulus, thus lowering intraglomerular pressure and hyperfiltration, conferring renoprotective benefits[4]. DPP4 inhibitors like sitagliptin are also shown to maintain glycemic control without inducing notable fluid or electrolyte disturbances and are suitable for early to moderate CKD stages [10].

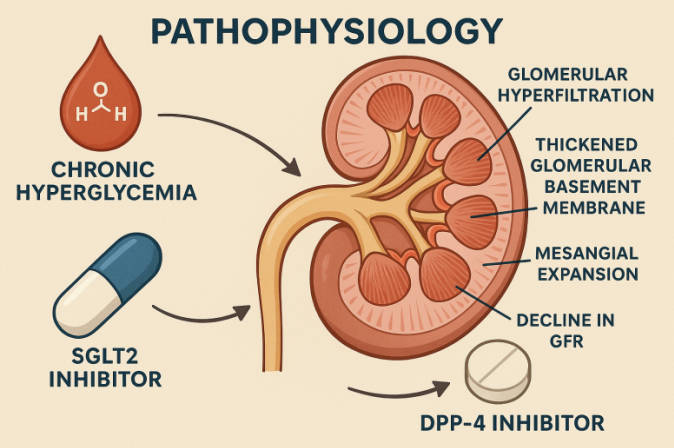

Figure. 1

CLINICAL MANIFESTATIONS

Patients typically experience polyuria, fatigue, and swelling in lower limbs. Laboratory manifestations are proteinuria, raised serum creatinine, and lowered eGFR. Hyperkalemia and metabolic acidosis can feature in established cases. Urinary tract infections and genital infections are common in patients on SGLT2 inhibitors[2]. Anemia is frequently seen in late-stage CKD. Other signs include nocturia and poor wound healing. Blood pressure elevation is a common finding. Cardiovascular symptoms may accompany renal dysfunction. Neuropathy may coexist with nephropathy.

IMPORTANCE

Effective management of glycemic control in renal-compromised patients improves outcomes. The use of SGLT2 inhibitors has been associated with cardiovascular and renal benefits. DPP-4 inhibitors provide an alternative with fewer electrolyte-related risks. Understanding drug safety profiles helps prevent adverse effects like AKI and hyperkalemia[1] . Comparative evaluation guides better drug selection. Proper therapy selection can prevent hospitalizations. Minimizing side effects improves adherence. Therapeutic success depends on early intervention. Evidence-based guidelines are critical. Precision medicine approaches are increasingly important.

MANAGEMENT OF T2DM AND KIDNEY DISEASE

The care of patients with both CKD and T2DM should involve an integrated strategy incorporating lifestyle, glycemic management and renal protection. Blood pressure control with RAAS inhibitors, glycemic regulation using renal-safe antidiabetics, and lipid management form the cornerstone of therapy. Dapgliflozin has demonstrated considerable benefits in delaying the progression of kidney disease and minimizing cardiovascular events in patients with diabetes and CKD[3]. Sitagliptin, being safe and effective in elderly patients and those with mild renal impairment, is also a recommended option[6]. It is important to stay away from drugs that can aggravate renal dysfunction and to monitor kidney parameters regularly. Multidisciplinary management with nephrologists, endocrinologists and clinical pharmacists enhances outcomes and reduces hospitalization. Due consideration must also be paid to complications like electrolyte imbalance and infection risk, particularly in patients on SGLT2 inibitors [Gential infections, Urinary tract infection, hypotension risk, dehydration [2]].

PHARMACOLOGICAL APPROACHES

Pharmacologic therapy in T2DM with kidney disease needs to be tailored according to kidney disease comordities, and risk factors. SGLT2 inhibitors such as dapagliflozin provide glycemic and renoprotective effects and are currently being advocated as first-line therapy in T2DM patients with CKD [2]. They also decrease the risk of heart failure and end-stage renal disease progression. DPP-4 inhibitors like sitagliptin are weight neutral and have less risk of hypoglycemia and are suitable for elderly or patients who cannot tolerate volume shifts[5]. Recent meta-analyses have shown that dapagliflozin reduces albuminuria and maintains eGFR in heterogeneous populations[4]. Monitoring and dose adjustment are essential, and choice should be based not only on efficacy but also on patient tolerability and possible side effects [10].

MECHANISM OF ACTION OF DRUGS USED

Sitagliptin is a dipeptidyl peptidase-4(DPP-4) inhibitor that functions by inhibiting the breakdown of incretin hormones, such as GLP-1 and GIP. These hormones stimulate insulin release and suppress glucagon release after meals. Sitagliptin enhances their activity, improving glycemic control without producing hypoglycemia, particularly when used alone or with metformin. Sitagliptin is well tolerated and neutrally affects body weight. Sitagliptin is useful in patients with mild and moderate renal impairment and must be dosed accordingly based on kidney function[5]. Additionally, sitagliptin has been noted to have a good safety profile with decreased risk of hypoglycemia and acceptable side effects in elderly and geriatric populations[6]. Dapagliflozin is in the class of sodium-glucose cotransporter-2 (SGLT2) inhibitors. It exerts its action by blocking the SGLT2 protein, thus decreasing glucose rea in the proximal renal tubules, thus decreasing glucose reabsorption and enhancing urinary glucose excretion. This action decreases blood glucose levels without being dependent on insulin and is therefore useful in states of chronic insulin resistance. Dapagliflozin also facilitates minimal weight loss and reduction in blood pressure through osmotic diuresis. It has renal protection and cardiovascular effects, especially in patients with established CKD or heart failure[4]. However, the medication has certain side effects such as genital infection, urinary tract infection, risk of hypotension and dehydration [2]. These are more significant in volume-depleted patients and the elderly. Both sitagliptin and dapagliflozin are significant pharmacological choices of T2DM treatment with renal impairment, each with its own mechanism and advantages. Choice of therapy should take into account renal function, cardiovascular status, tolerability, and risk of adverse effects as noted in some clinical trials [3] [10].

RISK AND BENEFITS OF SITAGLIPTIN

Sitagliptin is low risk for hypoglycemia. It is also weight neutral and easy to use in combination therapy. There is risk pf acute kidney injury and pancreatitis [10]. Hypersensitivity reactions like rash or anaphylaxis are rare. Beneficial for those who cannot tolerate other medications that reduce blood sugar levels. No substantial effect on lipid profile. Can be continued safely in early CKD stages. Suitable for elderly or polypharmacy patients. May have neutral cardiovascular impact. Long-term studies support safety in moderate renal dysfunction.

RISK AND BENEFITS OF DAPAGLIFLOZIN

Dapagliflozin provides substantial cardiovascular and kidney protection[4]. It is weight-reducing and blood pressure-lowering. The risk of dehydration, UTIs, and urethral infections may increase as a result. [2]. Patients should be counseled on maintaining hydration. Avoid use in those with frequent urinary infections. May reduce hospitalization for heart failure. Improves outcomes in CKD with or without diabetes. Ketoacidosis risk is rare but significant. Diuretic-like action may enhance blood pressure control. Tolerability is good in most adult populations.

CLINICAL ASSESSMENT INCLUDED

- Kidney Function Tests: Urea, Serum creatinine, Uric acid to assess kidney function and disease progression.
- Electrolyte Monitoring: Serum potassium levels to assess the risk of hyperkalaemia.
- Glycemic Control: Haemoglobin A1c (HbA1c) levels to assess blood sugar control.
- Adverse Effects Monitoring: Regular monitoring for adverse effects such as hypoglycemia, volume depletion, and diabetic ketoacidosis.

RESULT

Both sitagliptin and dapagliflozin is used in the improvement of glycemic control in CKD patients. Dapagliflozin showed added benefit in slowing kidney disease progression. Sitagliptin was associated with fewer genitourinary side effects. Dapagliflozin reduced cardiovascular events and hospitalizations. Sitagliptin was better tolerated in elderly patients[6]. Combination therapies had no added renal risk. HbA1c reduction was similar in mild CKD. Dapagliflozin reduced albuminuria significantly. AKI rates were low with appropriate monitoring. No significant increase in hypoglycemia with either agent.

CLINICAL IMPLICATIONS

Drug selection should consider renal status and cardiovascular history. Dapagliflozin is preferred for patients needing renal and CV protection. For old and weak people, sitagliptin is safer. Monitoring for side effects is essential, especially genitourinary infections. Adjust treatment based on lab parameters and clinical response. Shared decision-making improves compliance. Dose adjustment is key to prevent toxicity. Both agents support patient-centered care. Real-world data support effectiveness. Multidisciplinary follow-up is ideal.

FUTURE DIRECTIONS

Further trials comparing long-term outcomes of both drugs are needed. Combination therapies may enhance efficacy and reduce risk. More real-world studies in high-risk populations will improve clinical guidelines. Biomarkers to predict response to treatment could enhance personalization. Approaches for handling side effects can improve adherence[7]. Development of renal-safe drug combinations is ongoing. Genetic studies may identify at-risk populations. Pharmacovigilance must be enhanced. Comparative cost-effectiveness analyses are warranted. Digital tools can support medication adherence.

DISCUSSION

This comparative review underscores dapagliflozin's advantages in cardiorenal protection. Sitagliptin remains a reliable option with a favorable safety profile. Clinician decisions should integrate patient-specific risks, comorbidities, and tolerability. The evidence supports SGLT2i as frontline therapy in suitable patients. Ongoing surveillance and research are needed for optimal results. Patient quality of life is better with right choice. Emerging data continue to refine clinical pathways. Use of both agents is supported in different contexts. More individualized therapy is the future of diabetes care. Clinical inertia must be overcome with strong evidence.

CONCLUSION

In conclusion, both Dapagliflozin and sitagliptin are worth therapeutic tools for the treatment of type2 diabetes mellitus in renal-impaired patients. Dapagliflozin exihibits substantial advantages in terms of cardiovascular and renal protection, making it a best choice in patients with established kidney disease or those at high cardiovascular risk. But its use demands careful monitoring for possible genitourinary infections and volume depletion. Sitagliptin, however, has a safer profile in elderly or frail patients, especially where dehydration or urinary tract infection risk is a factor. Its tolerability and favorable profile for risk of hypoglycemia make it a sensible choice for long treatment. Individualized therapy, based on patient attributes, comorbidities, and kigney function, is essential to the attainment of optimal results. Combination of clinical practice guidelines, patient education, and multidisciplinary management potentiates the efficacy of treatment protocols. Additional studies, such as real-world experience and long-term outcome trials, must be conducted to define absolute therapeutic choices. Clinicians should also take into consideration cost, and adherence when selecting therapy.

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