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CASE REPORT

Drug-induced hypoglycemia in a patient with Type 2 diabetes and renal impairment: A case report

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Abstract

Hypoglycemia is a serious adverse effect in the pharmacological treatment of Type 2 diabetes mellitus (T2DM), exacerbated by comorbidities that affect drug metabolism and clearance. This report describes a case involving a 61-year-old man with hypertension and T2DM. The patient experienced hypoglycemia while taking a combination of voglibose and metformin hydrochloride. His condition was further complicated by urosepsis, acute-on-chronic kidney disease, and hydroureteronephrosis calculi, which likely altered drug clearance and pharmacokinetics. This condition increased his risk of hypoglycemia. Effective management required close monitoring of blood glucose levels and adjustments to the treatment regimen, considering his renal impairment. This case highlights the risks associated with combination therapy in patients with renal issues and underscores the importance of personalized treatment plans, vigilant glucose monitoring, and consideration of renal function to reduce the risk of drug-induced hypoglycemia in patients with T2DM and comorbidities.

Keywords: Hypoglycemia; Combination therapy; Renal impairment; Glycemic control; Type 2 diabetes mellitus

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1. Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by high blood glucose levels due to insufficient insulin production or ineffective insulin action. It is a global health concern, affecting approximately 463 million adults worldwide in 2019, and the prevalence projected to increase to 700 million by 2045.[1] In managing Type 2 diabetes mellitus (T2DM), optimal glycemic control must be maintained to prevent complications such as cardiovascular disease, nephropathy, retinopathy, and neuropathy.[2]

Pharmacotherapy is essential for achieving glycemic control in patients with T2DM. Classes of antidiabetic agents, including biguanides, sulfonylureas, dipeptidyl peptidase-4 (DPP-4) inhibitors, and alpha-glucosidase inhibitors, target different pathways involved in glucose metabolism.[3] Combination therapy, involving the concurrent use of multiple antidiabetic agents with complementary mechanisms of action, is frequently employed to achieve better glycemic control in patients who do not respond adequately to monotherapy.[4,5]

However, the use of combination therapy in T2DM comes with risks. Hypoglycemia, one of the most concerning complications associated with antidiabetic agents, is characterized by abnormally low blood glucose levels. Hypoglycemia can have serious consequences, ranging from mild symptoms such as confusion and shakiness to severe neurological impairment, coma, or death if left untreated.[6,7] The risk of hypoglycemia is further increased in patients with renal impairment due to alterations in drug clearance and pharmacokinetics.[8,9]

Renal impairment is a common comorbidity in patients with T2DM, affecting approximately 40% of this patient population.[10,11] The kidneys are crucial in the elimination of drugs from the body, and any impairment in renal function can lead to the accumulation of drugs and their metabolites, potentially increasing the risk of adverse effects.[12] Moreover, in patients with renal impairment, dose adjustments and careful selection of antidiabetic agents must be considered to prevent drug-induced hypoglycemia or other adverse events.

Voglibose, an alpha-glucosidase inhibitor, delays the absorption of carbohydrates in the intestine, thereby reducing postprandial hyperglycemia.[13,14] Metformin, a biguanide, is commonly used as a first-line therapy in T2DM management owing to its ability to reduce hepatic glucose production and improve insulin sensitivity.[10,15] Both voglibose and metformin have shown efficacy in improving glycemic control; however, their use in combination therapy and the potential associated risks, particularly in patients with renal impairment, have not been extensively studied.[14,15]

This case report describes the clinical presentation of a 61-year-old male patient with a medical history of hypertension and T2DM. He developed hypoglycemia while taking a combination of voglibose and metformin hydrochloride for glycemic control. The patient also had a history of urosepsis, acute-on-chronic kidney disease (CKD), and hydroureteronephrosis calculi, which may have contributed to altered drug clearance and pharmacokinetics, thereby increasing the risk of hypoglycemia.

This case report primarily aimed to highlight the potential risks associated with combination therapy for diabetes, particularly in patients with renal impairment. This case underscores the importance of close monitoring of blood glucose levels and renal function in patients with T2DM and renal impairment to prevent drug-induced hypoglycemia. Another aim is to raise awareness among healthcare providers regarding the need for individualized treatment plans and cautious selection of antidiabetic agents in this patient population.

To the best of our knowledge, this is one of the few reported cases of hypoglycemia associated with the combined intake of voglibose and metformin hydrochloride in a patient with T2DM and renal impairment. The case highlights the challenges faced in achieving optimal glycemic control in patients with multiple comorbidities, in the presence of renal impairment. The findings from this case report contribute to the growing body of literature on the risks and considerations associated with combination therapy in patients with T2DM and renal impairment.

2. Case presentation

A 61-year-old man with a history of type 2 diabetes mellitus (T2DM) and hypertension presented to the hospital with diminished consciousness, slurred speech, and profuse sweating. His antidiabetic regimen included glimepiride (2 mg), metformin (500 mg), and voglibose (0.2 mg). Two months prior, the patient had experienced hydroureteronephrosis calculi, acute-on-CKD, and urosepsis (Tables 1 and 2).

Table 1. Patient characteristics and baseline parameters

Parameter	At presentation	At discharge/follow-up
Age	61 years	-
Sex	Male	-
HbA1c	9.4%	7.6%
Fasting glucose	50 – 70 mg/dL	110 – 130 mg/dL
Postprandial glucose	Not assessed	140 – 180 mg/dL
Serum creatinine	2.6 mg/dL	2.4 mg/dL
eGFR	26 mL/min/1.73 m² (Stage 3b CKD)	33 mL/min/1.73 m²
Blood urea nitrogen	60 mg/dL	Not reassessed
Comorbidities	Hypertension, CKD, and nephrolithiasis	-

Abbreviations: CKD: Chronic kidney disease; eGFR: Estimated glomerular filtration rate; HbA1c: Hemoglobin A1c.

Table 2. Medication regimens and adjustments

Therapy	Dosage	Indication	Outcome
Glimepiride	2 mg/day	T2DM	Discontinued due to hypoglycemia
Metformin	500 mg/day	T2DM	Discontinued due to CKD
Voglibose	0.2 mg/day	Postprandial glucose control	Discontinued
Linagliptin	5 mg/day	T2DM with CKD	Initiated, improved glycemic control
Losartan	50 mg/day	Hypertension	Continued
Amlodipine	5 mg/day	Hypertension	Continued
Atorvastatin	10 mg/day	Dyslipidemia	Continued

Abbreviations: CKD: Chronic kidney disease; T2DN: Type 2 diabetes mellitus.

2.1. Pathophysiological and clinical considerations

The combination of glimepiride, metformin, and voglibose increased the risk of hypoglycemia in this patient due to several factors (Table 3). The presence of renal impairment resulted in reduced clearance of glimepiride, thereby prolonging its hypoglycemic action. In addition, CKD diminishes gluconeogenesis, a key counterregulatory mechanism. While metformin and voglibose are not typically associated with hypoglycemia, their use in combination with sulfonylureas, particularly in patients with CKD, can potentiate this risk. Furthermore, the patient's renal impairment was likely exacerbated by his history of urosepsis and nephrolithiasis, which contributed to altered drug clearance and pharmacokinetics.

2.2. Post-intervention management and alternative therapy

After discontinuing the combination therapy, linagliptin, a DPP-4 inhibitor, was prescribed. In CKD, linagliptin is metabolized primarily by the liver and does not require dose adjustments, making it an appropriate choice for this patient.

On examination, the patient's vital signs were stable, and abdominal and systemic evaluations were unremarkable. Laboratory findings included high glycated hemoglobin (HbA1c) levels, indicating poor glycemic control, and renal function tests showed elevated creatinine and urea levels, indicative of renal impairment (Table 4).

The patient was diagnosed with hypoglycemia, with blood glucose levels ranging from 50 to 70 mg/dL. Immediate management involved a 25% dextrose infusion, which improved his consciousness and speech. Antacids led to symptomatic relief. Continuous glucose monitoring revealed improvement over the subsequent days.

The hypoglycemic episodes were attributed to an adverse drug reaction from the combination of glimepiride, metformin, and voglibose, compounded by the patient's impaired renal function. This therapy was discontinued, and an alternative regimen (linagliptin) was initiated.

The patient was diagnosed with hypoglycemia, with blood glucose levels ranging from 50 to 70 mg/dL. A 25% dextrose infusion was administered, which rapidly improved consciousness and speech. Antacids were also provided for symptomatic relief.

2.3. Renal function and glycemic outcomes (Tables 4 and 5)

2.3.1. Renal parameters

At presentation: Serum creatinine of 2.6 mg/dL, blood urea nitrogen of 60 mg/dL, and estimated glomerular filtration rate (eGFR) of 26 mL/min/1.73 m², consistent with acute worsening of stage 3b CKD.

At discharge: eGFR improved to 33 mL/min/1.73 m², and serum creatinine decreased to 2.4 mg/dL, reflecting partial renal recovery.

Table 3. Pathophysiological considerations of hypoglycemia

Factor	Mechanism	Effect on hypoglycemia
Reduced drug clearance	Impaired renal excretion of glimepiride	Prolonged hypoglycemic action
Decreased gluconeogenesis	CKD-related metabolic changes	Reduced endogenous glucose production
Combination therapy	Overlapping mechanisms of action	Potentiated risk of hypoglycemia

Abbreviation: CKD: Chronic kidney disease.

Table 4. Laboratory investigations

Test	Result at presentation	Normal range
Serum creatinine	2.6 mg/dL	0.6 – 1.2 mg/dL
eGFR	26 mL/min/1.73 m²	≥90 mL/min/1.73 m²
Blood urea nitrogen	60 mg/dL	7 – 20 mg/dL
HbA1c	9.4%	<7.0%
Hemoglobin	10.5 g/dL	13.5 – 17.5 g/dL (male)
Urine protein	+1	Negative
Fasting glucose	50 – 70 mg/dL	70 – 100 mg/dL

Abbreviations: eGFR: Estimated glomerular filtration rate; HbA1c: Hemoglobin A1c.

Table 5. Glycemic and renal function outcomes post-intervention

Parameter	Baseline (before change)	Follow-up (post-intervention)
HbA1c	9.4%	7.6%
Fasting glucose	50 – 70 mg/dL	110 – 130 mg/dL
Postprandial glucose	Not assessed	140 – 180 mg/dL
eGFR	26 mL/min/1.73 m²	33 mL/min/1.73 m²

Abbreviations: eGFR: Estimated glomerular filtration rate; HbA1c: Hemoglobin A1c.

2.4. Glycemic control (Tables 4 and 5)

Initial: HbA1c was 9.4%, and fasting glucose levels ranged from 50 to 70 mg/dL.

Post-intervention: HbA1c improved to 7.6% within 3 months. Fasting glucose levels stabilized at 110 – 130 mg/dL, and postprandial levels ranged from 140 to 180 mg/dL.

2.5. Additional clinical findings

2.5.1. Urine examination

Urine analysis showed mild proteinuria (+1) without microscopic hematuria. No growth was found on the urine culture, ruling out active infections. The history of nephrolithiasis and prior urosepsis was considered relevant to the baseline of patient with CKD.

2.5.2. Comorbidities and therapies

The patient had hypertension, which was managed with losartan and amlodipine, and dyslipidemia treated with atorvastatin. His HbA1c level was 10.5 g/dL, indicative of CKD-induced anemia.

2.5.3. Outcome and clinical implications

Glycemic control improved significantly without further hypoglycemic episodes. Linagliptin proved to be effective and safe, stabilizing blood glucose levels and preventing further renal compromise.

This case underscores the importance of individualized DM management in patients with renal impairment. Healthcare providers should carefully assess pharmacokinetics and comorbidities when selecting antidiabetic therapies to balance glycemic control with minimized adverse effects.

3. Discussion

This case report highlights the clinical challenges of managing a 61-year-old male patient with T2DM, hypertension, and CKD, emphasizing the recurrent hypoglycemic episodes associated with the combination therapy of glimepiride, metformin, and voglibose. The report underscores the need for tailoring antidiabetic therapy to individual patient factors such as renal impairment and comorbidities.

The combination of glimepiride, metformin, and voglibose is a widely used regimen for managing T2DM. Glimepiride, a sulfonylurea, stimulates pancreatic beta cells to release insulin, metformin, a biguanide, reduces hepatic glucose production and enhances insulin sensitivity, and voglibose, an alpha-glucosidase inhibitor, delays carbohydrate absorption, reducing postprandial glucose spikes. Despite their efficacy, these agents are associated with an increased risk of hypoglycemia, particularly in vulnerable populations such as those with CKD.

In this case, substituting linagliptin for the previous combination therapy effectively improved glycemic control and minimized the risk of hypoglycemia. Linagliptin is safe for the kidneys and aligns with current clinical guidelines for managing diabetes in patients with CKD. Post-intervention outcomes showed stable blood glucose levels and improved renal function, reinforcing the importance of selecting antidiabetic agents based on the patient's renal status and overall health condition.

The patient's medical history, including urosepsis, nephrolithiasis, and acute-on-CKD, complicated the challenges of drug clearance and pharmacokinetics. CKD can impair the excretion of medications, leading to drug accumulation and an increased risk of adverse effects. In this case, the combination therapy likely exacerbated the risk of hypoglycemia due to the reduced renal clearance of glimepiride and the impaired gluconeogenic capacity associated with CKD.

3.1. Pathophysiological mechanisms for increased hypoglycemia risk in CKD

Patients with CKD are particularly susceptible to hypoglycemia owing to the following mechanisms:

1. Reduced renal clearance of insulin: Impaired kidney function prolongs insulin half-life, increasing systemic levels.
2. Diminished gluconeogenesis: CKD compromises renal gluconeogenesis, a key counter-regulatory process in hypoglycemia prevention.
3. Coexistent malnutrition and anemia: CKD-associated anemia and reduced caloric intake lower glycogen stores and weaken hypoglycemia responses.
4. Enhanced sensitivity to hypoglycemic agents: Drugs such as sulfonylureas and insulin are cleared more slowly in CKD, amplifying their effects.

3.2. Assessing the cause of hypoglycemia

The patient had multifactorial hypoglycemic episodes, driven by both CKD-related alterations in metabolism and the pharmacodynamics of glimepiride, metformin, and voglibose. Glimepiride's prolonged action due to reduced renal clearance, coupled with impaired compensatory mechanisms such as gluconeogenesis, significantly contributed to the hypoglycemia observed.

3.3. Implications for clinical practice

T2DM management in CKD requires careful consideration of drug pharmacokinetics and potential adverse effects. Adjusting or discontinuing agents with a high hypoglycemia risk is essential to avoid complications. In this case, replacing the combination therapy with linagliptin improved glycemic control without inducing further hypoglycemia.

Regular monitoring of renal function and glycemic control, along with close patient–provider collaboration, is critical to ensure safe and effective diabetes and CKD

management. This case underscores the importance of individualized treatment plans that account for the interplay between diabetes and comorbid conditions.

3.4. Limitations

As a single-patient case report, these results cannot be generalized to all individuals with similar conditions. Differences in comorbidities, renal function, and pharmacogenetics may affect outcomes, emphasizing the need for a personalized approach to managing T2DM and associated comorbidities. This report contributes to the understanding of T2DM management in patients with CKD, offering valuable insights into optimizing therapeutic strategies while minimizing adverse effects.

4. Conclusion

This case report highlights the complexities of managing T2DM in patients with renal impairment and comorbidities, particularly the heightened risk of hypoglycemia associated with certain antidiabetic regimens. The recurrent hypoglycemic episodes experienced by the patient while taking a combination of glimepiride, metformin, and voglibose were attributed to altered drug clearance and pharmacokinetics resulting from renal dysfunction. Switching to linagliptin, a renal-friendly alternative antidiabetic agent, resulted in improved glycemic control and resolution of hypoglycemia. This case emphasizes the need to tailor diabetes management to individual patient needs, with careful consideration of comorbidities, regular monitoring of blood glucose levels, and assessment of renal function to prevent adverse outcomes and ensure safe and effective therapy.

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Conflict of interest

The authors declare that they have no competing interests.

Author contributions

Conceptualization: All authors
Investigation: All authors
Writing–original draft: All authors
Writing–review & editing: All authors

Ethics approval and consent to participate

Verbal and written consent was obtained from the patient before his participation.

Consent for publication

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Availability of data

Not applicable.

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