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# Enhanced glycemic control with triple diabetes medication: A case report

A 66-year-old male patient with a 7-year history of type 2 diabetes mellitus (T2DM) presented with suboptimal glycemic control (HbA1c 8.5%) despite previous treatment with metformin 1,000 mg and glimepiride 2 mg daily. The patient reported occasional episodes of hypoglycemia with his current treatment regimen. He reported he was nonadherent to the treatment due to concern about episodes of hypoglycemia.



## Medical history

- ⌘ Seven-year history of diabetes
- ⌘ One-year history of dyslipidemia managed with statin medication
- ⌘ Two-year history of hypertension which is well-controlled with antihypertensive medication



## Personal history

- ⌘ Retired teacher
- ⌘ Nonvegetarian
- ⌘ Sedentary lifestyle
- ⌘ Enjoys spicy and fried food



## Family history

- ⌘ Strong family history of diabetes with both parents having been diagnosed with T2DM in their late 50s.
- ⌘ Father had suffered a stroke at 70 years of age

# Diagnostic workup



## Physical examination



Height  
5'4"



Weight  
80 kg



BMI  
29 kg/m<sup>2</sup>

Body temperature	Heart rate	Blood pressure	Respiration rate	CV system
<b>Normal</b>	<b>78 bpm</b>	<b>130/85 mmHg</b>	<b>17 breaths/min</b>	<b>Normal</b>



## Laboratory investigations

### PARAMETERS

### FINDINGS

HbA1c	8.5%
Fasting blood glucose (FBG)	170 mg/dL
Postprandial blood glucose (PPG)	202 mg/dL
Lipid profile	Total cholesterol: 180 mg/dL
	HDL cholesterol: 45 mg/dL
	LDL cholesterol: 90 mg/dL
	Triglycerides: 170 mg/dL
Creatinine	0.9 mg/dL
Glomerular filtration rate (GFR)	105 mL/min/1.73 m <sup>2</sup>
Kidney function test	Within normal limits
Liver function tests	Within normal limits
Complete blood count	Within normal range



## Diagnosis

A known case of type 2 diabetes mellitus with hypertension and dyslipidemia.



## MANAGEMENT

### Non-pharmacological

- ⌘ **Dietary modifications:** He was advised to eat balanced diet that includes complex carbohydrates, lean proteins, healthy fats, and ample vegetables and fruits. He was also suggested to reduce sodium intake by avoiding processed food and salty snacks.
- ⌘ **Lifestyle modification:** Regular physical activity, such as walking, jogging, and some aerobic activities were recommended.

### Pharmacological

- ⌘ After a thorough evaluation of the patient's condition, it was decided to optimize glycemic control while minimizing the risk of hypoglycemia.
- ⌘ The patient's glimepiride dose was reduced to 1 mg daily to minimize the risk of hypoglycemia. Metformin was continued at 1000 mg daily.
- ⌘ Additionally, sitagliptin 100 mg once daily was initiated.
- ⌘ He was asked to continue with his antihypertensive and dyslipidemia medications.

### FOLLOW-UP

FOLLOW-UP

MONTH  
03

- ⌘ A remarkable improvement in blood glucose parameters was noted (Table 1).
- ⌘ He reported no hypoglycemic episodes.
- ⌘ He was advised to continue the combination of glimepiride 1 mg and metformin 1,000 mg twice daily along with sitagliptin 100 mg once daily.
- ⌘ Also, he was asked to continue with lifestyle changes and dietary modifications for better metabolic control.

FOLLOW-UP

MONTH  
06

- ⌘ The patient's progress continued to be positive at the 6-month follow-up session, with further improvements in glycemic control without hypoglycemic episodes. (Table 1).
- ⌘ The patient adhered to the new treatment regimen and made lifestyle changes, which contributed to the beneficial outcomes.
- ⌘ The patient was advised to continue with current medications and lifestyle modifications.

FOLLOW-UP

MONTH  
09

- ⌘ The patient's development remained positive, confirming the treatment plan as long-term viability (Table 1).
- ⌘ Throughout the treatment regimen, the patient did not experience any hypoglycemic episode.
- ⌘ The patient was encouraged to continue with lifestyle and dietary modifications for long-term results.

Table 1: Clinical and biochemical parameters at presentation and follow-up visits

Parameters	At presentation	At Month 3	At Month 6	At Month 9
Body weight (kg)	80	77	75	73
FBG (mg/dL)	170	145	127	102
PPG (mg/dL)	202	173	149	130
HbA1c (%)	8.5	7.9	7.2	6.9

FBG: Fasting blood glucose; PPG: Postprandial blood glucose.





## Discussion

Hypoglycemia is a usual complication in patients with diabetes.<sup>1</sup> Older patients with diabetes are at an increased risk of hypoglycemia due to factors such as weight loss, changing eating habits, declining renal function, age-related pathophysiological changes, etc. In addition to age-related changes, hypoglycemia is linked to the overtreatment of diabetes, and the use of antidiabetic medications such as insulin, sulfonylurea, or glinide.<sup>1,2</sup>

Therefore, the goal of pharmacological treatment of diabetes should be to achieve adequate glycemic control by preventing hypoglycemia and weight gain, hence lowering the risk of future micro- and macrovascular complications.<sup>3</sup> However, psychological factors like fear of hypoglycemia hinder glycemic control. Using glucose-lowering drugs that do not trigger excessive insulin secretion, such as metformin, sodium-glucose cotransporter-2 inhibitors (SGLT-2i), dipeptidyl peptidase-4 inhibitors (DPP-4i), glucagon-like peptide-1 receptor agonists (GLP1-RA), and thiazolidinediones, could be a wise approach to prevent complications and maintain good glycemic control.<sup>1</sup>

In the present case, the patient with long-standing diabetic reported occasional hypoglycemia and poor glycemic control due to previous treatment (metformin 1,000 mg and glimepiride 2 mg). To reduce hypoglycemia risk and enhance glycemic control, glimepiride dose was reduced to 1 mg and sitagliptin 100 mg (DPP-4 inhibitor) was added.



### WHAT DO GUIDELINES SAY?

The American Diabetes Association (ADA), Standards of Care in Diabetes - 2023 suggests the following:

- ⌘ In older adults with T2DM at increased risk of hypoglycemia, use of medication classes with low risk of hypoglycemia is preferred. Overtreatment of diabetes is common and to be avoided.<sup>4</sup>
- ⌘ To achieve and maintain glycemic goals, ADA recommends the use of metformin or agent(s) including combination therapy that provide adequate efficacy.<sup>5</sup>
- ⌘ Incretin-based therapies such as oral DPP-4i have intermediate efficacy with few side effects and minimal risk of hypoglycemia.<sup>4,5</sup>

### DID YOU KNOW?<sup>3</sup>

The South Asian Federation of Endocrine Societies recommends reducing the dose of sulfonylureas in case of hypoglycemic episodes and when starting DPP-4 inhibitors, especially in older patients and/ or those with renal failure.<sup>6</sup>

## WHAT DOES EVIDENCE SUGGEST?<sup>1</sup>

Large clinical studies have shown that sitagliptin is well tolerated as a monotherapy, an add-on therapy with metformin, or an initial combination with metformin or a sulfonylurea; reduces HbA1c levels, in addition to, fasting and postprandial glucose concentrations. According to these trials, sitagliptin in combination therapy reduced HbA1c in the range of 0.45–1.9%.

A case series of three patients reported reductions in HbA1c levels ranging from 2–5% after adding sitagliptin to metformin (>1000 mg) and sulfonylurea. These results are stronger than those reported in clinical trials, implying that triple drug therapy regimen with antidiabetic medications may have a synergistic effect rather than an additive effect.

After 3 months of triple-drug therapy, there was a significant improvement in glycemic control, with no hypoglycemic episodes. The patient was advised to continue with the metformin-glimepiride-sitagliptin combination alongside lifestyle changes. At 6- and 9-month follow-ups, glycemic parameters consistently improved, indicated by an HbA1c decrease from 8.5% to 6.9%, respectively. The patient tolerated and adhered well to the triple drug therapy.



### Expert Views

- ☞ Older adults are prone to develop hypoglycemia due to several factors, including age-related pathophysiological changes, increased comorbidities, duration of diabetes, polypharmacy, and use of antidiabetic medications such as insulin, sulfonylureas, and glinides.
- ☞ Triple drug regimen by addition of DPP-4i, such as sitagliptin, to metformin and sulfonylurea has shown greater improvement in glycemic parameters by remarkably reducing HbA1c levels.
- ☞ In the present case, the patient suffered from hypoglycemia with combination therapy of metformin and glimepiride. The patient's therapy was modified to a triple drug regimen by adding sitagliptin to metformin + glimepiride combination and reducing the dose of glimepiride. The therapy was well-tolerated and compliant.

### References

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