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Uncontrolled type 2 diabetes in middle-aged female: A case report

A 42-year-old female with diabetes for 3 years was presented to the clinic with complaints of uncontrolled diabetes symptoms. She reported increasing fatigue, excessive thirst, frequent urination, and an unintended weight gain over the past few months. These symptoms had been affecting her daily life, work, and overall well-being. She was prescribed metformin 1,000 mg/day and glimepiride 1 mg twice daily, but she frequently missed the doses and often forget to renew her prescription.

Medical history

- Three-year history of diabetes
- Six-months history of dyslipidemia
- No other major illness or history of surgery

Personal history

- Beautician
- Has sedentary lifestyle with minimal physical activity
- Diet primarily consists of fast foods and high-calorie snacks

Family history

- Significant family history of obesity, hypertension, and type 2 diabetes mellitus (T2DM)
- Her father had a history of multiple instances of myocardial infarction and hypertension.

Diagnostic workup

Physical examination

Height	Weight	BMI
5'4"	67 kg	32 kg/m^2

Body temperature	Heart rate	Blood pressure	Respiration rate	CV system
Normal	**78** bpm	**134/80** mmHg	**16** breaths/min	**Normal**

Investigations

PARAMETERS	FINDINGS
Resting electrocardiograph	Within normal limits

Laboratory investigations

PARAMETERS		FINDINGS
HbA1c		8.8%
Fasting blood glucose (FBG)		197 mg/dL
Postprandial blood glucose (PPG)		224 mg/dL
Serum creatinine		1.0 mg/dL
Thyroid function tests		Within normal limits
Liver function tests		Within normal limits
Urinalysis		Presence of glucose
Lipid profile	Total cholesterol	240 mg/dL
	Low-density lipoprotein cholesterol	170 mg/dL
	High-density lipoprotein cholesterol	40 mg/dL
	Triglycerides	200 mg/dL

Diagnosis

Poorly controlled type 2 diabetes mellitus with dyslipidemia.

MANAGEMENT

Non-pharmacological

- **Dietary modifications:** The patient was advised to create a balanced meal plan containing carbohydrates, proteins, and healthy fats. She was provided with a list of foods and ingredients categorized according to their macronutrient content to help her gain a clear understanding.
- **Lifestyle modifications:** She was suggested to incorporate small lifestyle changes, such as short walks during household tasks and engage in stress-relief activities, such as deep breathing and meditation.
- **Education and counseling:** The patient had a collaborative discussion on the importance of treatment adherence. She was also explained about the potential impact of diabetes on long-term health and well-being.

Pharmacological

- To manage her poor blood glucose levels due to non-adherence, a third agent, sitagliptin 100 mg/day was added to glimepiride 1 mg and metformin 1,000 mg combination.
- For dyslipidemia she was on atorvastatin 10 mg; she was recommended to continue with the same medication.
- As there were significant alterations in her non-pharmacological modifications, the patient was advised to monitor blood glucose levels thrice a week to observe the changes.
- Her follow-ups were scheduled every 3 months.

FOLLOW-UP

FOLLOW-UP MONTH 03

Follow-up at Month 3

- The patient reported a good adherence to the glimepiride and metformin combination as well as her other medications.
- HbA1c levels reduced to 8.4 from 8.8 (Table 1).
- She lost 1 kg of body weight and reported improvement in her energy level.
- She was advised to continue the same medications and follow-up regularly.

FOLLOW-UP MONTH 06

Follow-up at Month 6

- She could continue the medications without any reported concerns or adverse effects.
- HbA1c, FBG, PPG levels, and body weight declined notably.(Table 1).
- She was asked to continue with the same medication and lifestyle modifications.

FOLLOW-UP MONTH 09

Follow-up at Month 9

- Again, there was a notable improvement in her HbA1c levels and body weight (Table 1).
- Her weight was reduced to 61 kg.
- She reported resolution of symptoms and expressed satisfaction with the treatment.
- She was advised to continue with the same medication therapy and lifestyle modifications for further improvement.

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

Parameter	At presentation	At Month 3	At Month 6	At Month 9
Body weight (kg)	67	66	63	61
FBG (mg/dL)	197	178	157	140
PPG (mg/dL)	224	210	197	186
HbA1c (%)	8.8	8.4	7.9	7.4

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

Discussion

Many individuals with T2DM eventually require combination therapy to effectively manage their elevated blood sugar levels, as condition progresses. It is often recommended to use combination therapies that involve different drug classes with complementary mechanisms of action to achieve more robust glycemic control.[1]

One of the most commonly used dual combination glucose-lowering therapy in T2DM patients is the combination of metformin and sulfonylurea (SU). However, even this combination may not always suffice to attain or sustain adequate glycemic control, necessitating further treatment intensification. Unfortunately,

some patients may be hesitant to use insulin injections or may be concerned about the adverse effects such as edema and weight gain associated with thiazolidinediones, which can impact their treatment compliance and glycemic response. Therefore, there is a growing need for additional treatment options that can be added to metformin and SU regimens, helping patients avoid transition to insulin therapy.[1]

Sitagliptin is an orally administered dipeptidyl peptidase-4 (DPP-4) inhibitor that can be taken once-a-day. It has shown promise in improving glycemic control as an add-on therapy to either metformin or SU monotherapy, as well as in conjunction with metformin and SU combination therapy.[1]

In the current case, the patient with a 3-year history of diabetes was presented with elevated blood glucose levels, fatigue, lack of energy, frequent thirst, and urination. Her recent blood report revealed elevated cholesterol levels, further underscoring the presence of concurrent dyslipidemia. She was prescribed metformin 1,000 mg/day and glimepiride 1 mg twice-daily but was nonadherent to the course. This lack of response to the initial therapy

WHAT DOES GUIDELINES SAY?[2]

According to International Diabetes Federation recommendations:

- If a combination of a glucose-lowering drug alongside metformin falls short in achieving or maintaining the desired HbA1c target, it is advisable to introduce a third glucose-lowering drug.

- Triple-therapy using 3 oral glucose-lowering drugs can be explored as an effective approach before adding an injectable.

DID YOU KNOW?[3]

In an Indian study, 58% of cases favored combining oral antidiabetic drugs with a preference for fixed-dose combinations.

and poor glycemic control prompted the addition of a third agent, sitagliptin 100 mg/day, to the existing fixed-dose combination of glimepiride and metformin. Along with this, essential dietary advice and counseling was provided.

After 3 months, there was a significant decline in her HbA1c levels. Thus, she was advised to continue the same medications and lifestyle modifications. At the time of second follow-up, after 6 months of triple-drug therapy, the patient reported a notable positive change in her condition. Her HbA1c levels dropped to 7.9, affirming treatment efficacy. At 9 months, the patient reported compelling results, which led to HbA1c improvement to 7.4, marking significant glycemic control progress.

WHAT DOES EVIDENCE SUGGEST?[1]

- Retrospective cohort analyses were conducted to assess the efficacy of co-administering sitagliptin to patients with inadequate glycemic control following treatment with metformin and SU.
- The study evaluated the effectiveness of adding sitagliptin to existing therapy in terms of HbA1c and body weight changes over a 52-week period among a total of 9,802 patients.
- An addition of sitagliptin 100 mg once daily resulted in 5.5 mmol/mol (0.5%) HbA1c reduction ($p<0.001$) and 0.8 kg weight reduction at 1 year ($p<0.001$).
- Sitagliptin demonstrated its effectiveness in patients who had suboptimal glycemic control with metformin, SU, or dual therapy, with the maximum efficacy observed between Weeks 36 and 48.

Expert Views

- In T2DM management, combination therapies with diverse mechanisms are often needed as the disease progresses.
- Metformin and SU combination is commonly used but may not always suffice, leading to a demand for additional options to avoid insulin therapy.
- Sitagliptin, a once-daily DPP-4 inhibitor, offers promise as an add-on treatment to enhance glycemic control in various T2DM regimens.
- Retrospective analysis demonstrated that addition of sitagliptin as a third agent to the fixed-dose combination of SU and metformin resulted in good glycemic control.

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