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Metformin-Induced Irritable Bowel Syndrome–Like Symptom

Keywords: Metformin intolerance; irritable bowel syndrome; Type 2 diabetes mellitus; Dapagliflozin; SGLT2 inhibitors

Abstract

Metformin is the first-line pharmacological therapy for type 2 diabetes mellitus (T2DM). Although gastrointestinal (GI) adverse effects are common, persistent symptoms resembling irritable bowel syndrome (IBS) are less frequently reported. We present the case of a 56-year-old male with T2DM who developed metformin-induced IBS-like symptoms (IBS -D) characterized by abdominal cramping, bloating, and postprandial diarrhoea triggered by specific dietary factors. Symptoms significantly worsened following metformin dose escalation from 500 mg to 750 mg daily. Laboratory evaluation revealed adequate glycemic control with fasting blood glucose of 140 mg/dL and HbA1c of 6.5%. After discontinuation of metformin and initiation of dapagliflozin 10 mg daily along with dietary modification, gastrointestinal symptoms markedly improved while glycemic control remained stable. This case highlights the importance of recognizing metformin-induced IBS-like symptoms and considering alternative antidiabetic therapies when intolerance occurs.

Introduction

Metformin remains the cornerstone of therapy for type 2 diabetes mellitus (T2DM) because of its well-established efficacy, favourable safety profile, and low cost. Current clinical guidelines recommend metformin as the first-line pharmacotherapy for most patients with T2DM. Despite its overall favourable profile, gastrointestinal intolerance represents the most frequently reported adverse effect associated with metformin therapy. Approximately 20–30% of patients receiving metformin experience gastrointestinal symptoms, including diarrhea, abdominal discomfort, nausea, and bloating.

In most cases, these adverse effects are mild and transient. However, in some individuals, persistent gastrointestinal disturbances may develop that closely resemble symptoms of irritable bowel syndrome (IBS). Such symptoms can significantly affect quality of life and lead to poor medication adherence or discontinuation. Recognition of medication-induced gastrointestinal symptoms is therefore essential in the management of diabetic patients presenting with chronic bowel complaints. This report describes a case of **dose-dependent metformin intolerance presenting with IBS-like symptoms**, which improved after discontinuation of metformin and initiation of dapagliflozin.

Case Presentation

A 56-year-old male with a three-year history of type 2 diabetes mellitus presented with chronic gastrointestinal complaints consisting of intermittent abdominal cramping, bloating, and loose stools occurring two to three times daily, associated with postprandial urgency. The symptoms were particularly triggered by the consumption of spicy foods, coffee, and red meat.

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The patient had no prior history of gastrointestinal disease, inflammatory bowel disease, or food allergies. He denied weight loss, hematochezia, nocturnal diarrhea, fever, or other systemic symptoms.

Medical History

The patient had been diagnosed with type 2 diabetes mellitus three years earlier and was initially treated with extended-release metformin (**metformin XR) 500 mg once daily**. During this period, he reported mild intermittent loose stools, which were tolerable and did not interfere with daily activities.

Due to suboptimal glycemic control, the metformin XR dose was increased to **750 mg daily**. Within two to three weeks following dose escalation, the patient experienced a significant worsening of gastrointestinal symptoms, including:

- Increased stool frequency (four to five times per day)
- Marked abdominal discomfort
- Postprandial urgency
- Exacerbation of symptoms after consumption of spicy food, coffee, and red meat

The patient had no history of hypertension or dyslipidemia. He was a non-smoker and reported occasional alcohol consumption.

Laboratory Investigations

Laboratory evaluation revealed the following findings:

- Fasting blood glucose: 140 mg/dL
- HbA1c: 6.5%
- Complete blood count: within normal limits
- Liver function tests: normal
- Thyroid function tests: normal

The HbA1c and FBG results were verified using the formula: **Estimated Average Glucose (eAG) = (28.7 × HbA1c) − 46.7**, as described by M. Nathan et al. Investigations including *H. pylori*

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testing, stool culture, stool routine examination, and barium X-ray were performed and showed no evidence of infection, inflammatory disease, or metabolic abnormalities. Colonoscopy was not indicated, as there was no rectal bleeding and no abnormalities were observed on the X-ray.

The temporal association between the escalation of the metformin dose and the worsening of gastrointestinal symptoms, together with the absence of alarm features, strongly suggested **metformin-induced IBS-like gastrointestinal intolerance**.

Management

Considering the suspected drug intolerance, the following management strategy was implemented:

1. Discontinuation of metformin
2. Initiation of **dapagliflozin 10 mg once daily**
3. Dietary modification, including avoidance of known symptom-triggering foods

Following these interventions, the patient reported **marked improvement in gastrointestinal symptoms**. Stool frequency returned to normal, and abdominal discomfort resolved.

Glycemic control remained satisfactory with:

- Stable **HbA1c of 6.5%**
- Acceptable fasting glucose levels

Discussion

Metformin is widely recommended as the first-line therapy for T2DM because of its efficacy, low risk of hypoglycemia, and beneficial metabolic effects. However, gastrointestinal intolerance remains the most common adverse effect and may limit long-term adherence in some patients.

Mechanisms of Metformin-Induced Gastrointestinal Symptoms

Several mechanisms have been proposed to explain metformin-associated gastrointestinal intolerance.

1. Alteration of Gut Microbiota

Metformin significantly alters intestinal microbiota composition. Studies have demonstrated an increased abundance of bacterial species such as *Akkermansia muciniphila* and *Escherichia* species. Although these microbial changes may improve glucose metabolism, they may also increase intestinal fermentation and gas production, contributing to bloating and abdominal discomfort.

2. Increased Intestinal Glucose Metabolism

Metformin enhances intestinal glucose uptake and anaerobic metabolism, resulting in increased lactate production within enterocytes. This process may contribute to intestinal irritation and diarrhea.

3. Bile Acid Malabsorption

Metformin may interfere with bile acid reabsorption in the ileum. Increased bile acid concentrations in the colon stimulate intestinal secretion and motility, resulting in diarrhea resembling IBS.

Table 1: Comparative Overview of Antidiabetic Drug Classes

Feature	Metformin	SGLT2 Inhibitors	GLP-1 Receptor Agonists
Primary Mechanism	Decreases hepatic glucose production and improves insulin sensitivity	Blocks renal glucose reabsorption in proximal tubule	Increases insulin secretion and reduces glucagon
Effect on Weight	Neutral or mild weight loss	Mild weight loss	Significant weight loss
Gastrointestinal Effects	Common	Rare	Common during initiation
Cardiovascular Benefit	Moderate	Strong evidence	Strong evidence
Route of Administration	Oral	Oral	Mostly injectable

4. Serotonin Signalling in the Gut

Metformin may increase serotonin release from enterochromaffin cells, which plays a critical role in regulating intestinal motility and visceral sensitivity. Enhanced serotonin activity may therefore contribute to IBS-like symptoms.

5. Effects on GLP-1 Secretion

Metformin increases endogenous glucagon-like peptide-1 (GLP-1) secretion. Although this contributes to improved glycemic control, it may also influence gastrointestinal motility and appetite regulation.

Role of Dietary Triggers

Dietary factors may exacerbate gastrointestinal symptoms in patients with metformin intolerance. Spicy foods can stimulate intestinal motility, while coffee increases colonic activity through caffeine-mediated hormonal effects. High-fat foods such as red meat may delay gastric emptying and worsen bloating and abdominal discomfort. In the present case, these dietary triggers significantly intensified the patient's symptoms.

Alternative Antidiabetic Therapy

SGLT2 Inhibitors

After discontinuation of metformin, the patient was treated with **dapagliflozin**, a sodium-glucose co-transporter-2 (SGLT2) inhibitor. SGLT2 inhibitors lower blood glucose by inhibiting renal glucose reabsorption in the proximal renal tubule, thereby promoting urinary glucose excretion. Because their mechanism of action is independent of gastrointestinal absorption, they are less likely to cause gastrointestinal adverse effects.

Additional benefits include:

- Modest weight loss
- Reduction in systolic blood pressure
- Cardiovascular and renal protection

The **DECLARE-TIMI 58 trial** demonstrated that dapagliflozin significantly reduced hospitalization for heart failure and slowed the progression of chronic kidney disease.

GLP-1 Receptor Agonists

Another therapeutic option for patient's intolerant to metformin

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is the class of **GLP-1 receptor agonists**, including liraglutide and semaglutide.

These agents improve glycemic control by:

- Enhancing glucose-dependent insulin secretion
- Suppressing glucagon release
- Delaying gastric emptying
- Increasing satiety and promoting weight loss

However, GLP-1 receptor agonists frequently cause gastrointestinal adverse effects, particularly nausea and vomiting during treatment initiation. Therefore, they may not be ideal for patients with significant baseline gastrointestinal intolerance.

Clinical Implications

This case emphasizes the importance of recognizing **drug-induced gastrointestinal symptoms** in patients with diabetes. IBS-like symptoms occurring during metformin therapy may be misinterpreted as primary functional bowel disease, potentially leading to unnecessary diagnostic investigations.

Careful assessment of the **temporal relationship between medication exposure and symptom onset** is essential in identifying medication-related adverse effects.

Management strategies may include:

- Gradual dose titration
- Use of extended-release formulations
- Dietary modification
- Dose reduction or discontinuation
- Switching to alternative drug classes such as **SGLT2 inhibitors or GLP-1 receptor agonists**

Patient Perspective

Following discontinuation of metformin and initiation of dapagliflozin therapy, the patient reported significant relief from gastrointestinal symptoms. He expressed satisfaction with the new treatment regimen, noting improved daily comfort, reduced bowel urgency, and better adherence to diabetes therapy. He was also able to consume previously triggering foods such as spicy dishes, red meat, and coffee without recurrence of gastrointestinal symptoms.

Learning Points

1. Metformin remains the first-line therapy for type 2 diabetes but frequently causes gastrointestinal adverse effects.

2. In some patients, metformin intolerance may present with IBS-like symptoms such as abdominal pain, bloating, and diarrhea.

3. Symptoms may worsen after dose escalation of metformin.

4. Dietary triggers such as spicy foods, caffeine, and high-fat meals may exacerbate metformin-induced gastrointestinal symptoms.

5. Alternative therapies such as **SGLT2 inhibitors** can provide effective glycemic control in patients who cannot tolerate metformin.

Conclusion

Metformin-induced gastrointestinal intolerance may occasionally present with IBS-like symptoms, particularly following dose escalation. Clinicians should consider medication-related causes when diabetic patients develop new-onset chronic gastrointestinal complaints.

In this case, discontinuation of metformin and initiation of dapagliflozin successfully resolved gastrointestinal symptoms while maintaining adequate glycemic control. Recognition of metformin intolerance and timely adjustment of therapy can improve patient adherence, quality of life, and long-term diabetes management.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying clinical information.

Conflict of Interest

The author declares no conflict of interest related to this manuscript.

Ethical Considerations

This case report was conducted in accordance with ethical principles. Institutional approval was not required for a single anonymized case report.

References

1. McCreight LJ, Bailey CJ, Pearson ER (2016) Metformin and the gastrointestinal tract. *Diabetologia* 59:426-435.
2. Bailey CJ, Turner RC (1996) Metformin. *New England Journal of Medicine*. 1996;334: 574-579.
3. Forslund K, Hildebrand F, Nielsen T, Falony G, Chatelier EL, et al. (2107) Disentangling type 2 diabetes and metformin treatment signatures in the human gut microbiota. *Nature 528: 262-266*.
4. Zinman B, Lachin JM, Inzucchi SE (2015) Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *New England Journal of Medicine 374: 1094*.
5. Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, et al. (2019) Dapagliflozin and cardiovascular outcomes in type 2 diabetes. *New England Journal of Medicine* 380: 347-357.
6. Marso SP, Daniels GH, Brown-Frandsen K, Kristensen P, Mann JFE, et al. (2016) Liraglutide and cardiovascular outcomes in type 2 diabetes. *New England Journal of Medicine*.375: 311-322.
7. Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, et al. (2008) Associations between features of glucose exposure and A1C: the A1C-Derived Average Glucose (ADAG) study Diabetes 59: 1585-1590.