WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

METFORMIN-ASSOCIATED CHRONIC DIARRHEA LEADING TO SIGNIFICANT WEIGHT LOSS: A CASE REPORT FROM A TERTIARY CARE HOSPITAL

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ABSTRACT :

Metformin, a first-line biguanide for Type 2 Diabetes Mellitus, commonly causes transient gastrointestinal side effects. However, chronic diarrhea due to long-term use is rare. We report a 38-year-old male with persistent diarrhea and unintentional weight loss after two years on Metformin, which resolved upon drug withdrawal and insulin initiation. This case highlights the importance of pharmacovigilance and early recognition of adverse drug reactions in primary care.

Keywords: Metformin, Chronic Diarrhea, Pharmacovigilance, Adverse Drug Reaction, Type 2 Diabetes Mellitus

Introduction

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder with a global prevalence of 10.5% in adults aged 20–79 years, and India is considered the diabetes capital of the world[1]. Metformin, a biguanide, remains the first-line oral antidiabetic drug recommended by the American Diabetes Association (ADA) and Indian Council of Medical Research (ICMR) due to its ability to improve insulin sensitivity, lower hepatic glucose production, and reduce cardiovascular risk[2].

Despite its favourable safety profile, Metformin is associated with gastrointestinal adverse drug reactions (ADRs), which include abdominal discomfort, nausea, vomiting, and diarrhea[3]. These reactions are generally transient and dose-related, occurring within the first few weeks of initiation. Chronic diarrhoea due to long-term Metformin therapy is less commonly documented and often overlooked in primary care settings[4]. Persistent gastrointestina1 intolerance may lead to discontinuation of therapy, poor glycaemic control, and unnecessary diagnostic investigations[5].

We report a case of chronic diarrhoea due to prolonged Metformin use in a patient with T2DM, emphasizing the need for early detection, proper management, and reporting under the Pharmacovigilance Programme of India (PvPI).

Case Presentation

A 38-year-old male (patient initials: BR), weighing **50 kg before illness** and currently **39 kg**, known case of T2DM for the past three years, presented to the General Medicine Department at Government Medical College and Hospital, Orathur, Nagapattinam, with complaints of persistent diarrhoea for the past six months. The diarrhoea was characterized by 4–5 loose, watery stools per day, associated with mild, diffuse abdominal discomfort. There was no passage of blood or mucus. The patient also reported progressive, unintentional weight loss of approximately 4–5 kg over six months.

There was no history suggestive of infectious etiology, including recent travel, food poisoning, or exposure to unsafe water. He denied the use of antibiotics, alcohol, herbal medications, or over-the-counter supplements. His past medical history was unremarkable apart from T2DM for three years, for which he had been receiving Metformin 500 mg twice daily for the past two years, initiated at a Primary Health Centre. No other antidiabetic drugs had been prescribed during this time. The onset of diarrhoea was insidious and persisted despite dietary modifications, probiotics, and other symptomatic treatments.

On physical examination, the patient appeared mildly dehydrated but alert and oriented. He was afebrile, with stable vital signs: blood pressure 110/70 mmHg, pulse 84/min, respiratory rate 18/min, and oxygen saturation of 98% on room air. Abdominal examination revealed mild diffuse tenderness without organomegaly, guarding, or rebound tenderness. Cardiovascular, respiratory, and neurological examinations were normal.

Laboratory Findings

PARAMETER	VALUE	REFERENCE RANGE	UNITS
Haemoglobin (Hb)	11.2	13.5–17.5	g/dl
White Blood Cells (WBC)	21.7	4.0–11.0	$x10^3/\mu l$
Lymphocytes	44	20–40	%
Neutrophils & Monocytes	↑	40–75 & 2–8	%
Platelets (PLT)	222	150–400	$x10^3/\mu l$
RBC	4.08	4.2–5.9	$x10^6/\mu l$
Sodium	140	135–145	mEq/L
Potassium	3.4	3.5–5.0	mEq/L

Vitamin B_{12} levels often decrease with long-term Metformin use[6]. Stool examination was negative for ova, cysts, or pathogenic bacteria. Colonoscopy findings were unremarkable.

Management and Outcome

Metformin was discontinued, and the patient was switched to Human Insulin. Within two weeks, the frequency of diarrhoea reduced significantly. At follow-up after one month, the patient reported complete resolution of symptoms with good glycaemic control.
Chronic diarrhoea was managed by stopping metformin, providing hydration, electrolyte correction, dietary advice, and probiotics. For glycaemic control, the patient was started on insulin therapy, leading to resolution of diarrhoea and good blood sugar control. Supportive therapy was also provided for mild dehydration and the risk of electrolyte imbalance, with close monitoring of HbA1c and weight.

WHO-UMC Causality Assessment

According to the WHO-UMC scale, the ADR was categorized as "Probable / Likely" because:

There was a reasonable temporal association with Metformin use.
The reaction improved upon withdrawal of the drug.
No alternative explanation was found[7].

Role of Pharmacist

Clinical pharmacists play a crucial role in identifying adverse drug reactions, educating patients about possible side effects, and reporting ADRs to national pharmacovigilance programs like PvPI[8]. In this case, timely identification and reporting of the reaction by the PharmD intern contributed to appropriate management and prevention of further complications. Pharmacists also support dose adjustment, suggest safer alternatives, and ensure medication safety through continuous monitoring.

Discussion

Metformin-induced diarrhoea is typically observed during the initiation phase; however, chronic diarrhoea after long-term use is rare and underreported[9].
The proposed mechanisms include:

1. Increased intestinal glucose turnover causing osmotic diarrhoea.
2. Alteration of gut microbiota leading to malabsorption.
3. Bile salt malabsorption due to interference with enterohepatic circulation.
4. Inhibition of intestinal serotonin transporter, affecting motility.

Risk factors for severe gastrointestinal ADRs include higher doses, prolonged therapy, low BMI, and concurrent renal impairment[10]. Persistent diarrhoea may cause dehydration, electrolyte imbalance, and poor adherence to therapy, ultimately worsening glycaemic control.
The present case underscores the importance of ADR reporting to PvPI, as such reports contribute to signal detection and improved patient safety[11].

Conclusion

Chronic diarrhoea due to long-term Metformin therapy, although uncommon, can significantly affect patient compliance and quality of life. Early recognition, prompt discontinuation of the offending drug, and initiation of suitable alternative antidiabetic therapy are crucial to prevent unnecessary morbidity. Supportive measures such as hydration, electrolyte correction, dietary modifications, and probiotics should be provided to aid recovery. Regular monitoring of glycaemic status and nutritional assessment ensures better outcomes. Furthermore, reporting ADRs to pharmacovigilance centers enhances patient safety and strengthens drug safety databases.

Consent and Ethical Considerations

Written informed consent was obtained from the patient's legal guardian for publication of this case report and related clinical information. As per institutional policy, ethical approval was not required for anonymized single-patient case reports. The authors declare no conflicts of interest.

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