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Case Study

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# A Common Drug Causing a Common Side Effect at an Uncommon Time: Metformin-Induced Chronic Diarrhea and Weight Loss After Years of Treatment

*Karthik Subramaniam,[1] Manoj P Joseph,[2] and Lakshmi A Babu[2]*

## Background

Type 2 diabetes is a common condition, with a worldwide prevalence of 9.3% as of 2019 (1). Metformin is the most common drug used and is the first-line agent in type 2 diabetes management. It is also considered one of the safest pharmacological agents for the treatment of the disease. However, gastrointestinal side effects are common, occurring in up to 75% of those who take metformin (2). These side effects may include diarrhea, nausea, vomiting, abdominal discomfort, and/or flatulence, with severity ranging from mild to severe. These complications are more common with immediate-release preparations of metformin than with its extended-release formulation. Discontinuation and nonadherence rates have been as high as 46% with metformin because of these issues (3).

But still, metformin remains the first choice of medication for many insulin resistance syndromes because of its effect on weight. In the Diabetes Prevention Program research study (4), metformin reduced weight by a mean 2.9 kg, and this effect persisted up to 8 years. Metformin-associated weight loss begins with initiation of the medication and is beneficial in obese individuals with or without diabetes. However, weight loss can become an unintended adverse side effect in lean individuals with type 2 diabetes.

We report here a case series of patients with both adverse side effects—diarrhea and weight loss—that began after long-term use of metformin (Table 1) and provide a review of the related literature.

## Case Presentations

### *Case 1*

A 63-year-old woman known to have diabetes for 17 years with fair glycemic control presented with unintentional weight loss of 10 kg in the past year. She complained of intermittent, self-resolving, painless, small-volume, watery diarrhea and progressive dyspepsia for the same duration. She had a good appetite and healthy lifestyle. She was evaluated by a primary care physician, gastroenterologist, and psychiatrist for the above complaints and was referred as having diabetic diarrhea.

On evaluation, she was normotensive, with a BMI 0f 23.5 kg/m$^2$. She had no lymphadenopathy, and review of systems was unremarkable except for distal sensorimotor neuropathy in the lower limbs. Because of a concern of autonomic neuropathy, she was evaluated. Her electrocardiogram showed a sinus rhythm, there was no postural drop in blood pressure, and heart rate variability with deep breathing was normal.

A trial of metformin withdrawal was initiated. Within 1 week, she got better. At her last follow-up, she had gained weight, the diarrhea had stopped, and the dyspepsia had reduced. She was not achieving glycemic control with increasing doses of a sulfonylurea or a sodium–glucose cotransporter 2 (SGLT2) inhibitor and so was switched to a coformulation of insulin degludec and insulin aspart.

### *Case 2*

A 74-year-old woman with longstanding diabetes presented for management of type 2 diabetes. She had been having episodes of food-induced, mild, watery, solid, and unformed diarrhea with fecal incontinence for 1.5 years. She was evaluated thoroughly by a gastroenterologist, diagnosed with irritable bowel syndrome, and prescribed an antidepressant for its treatment.

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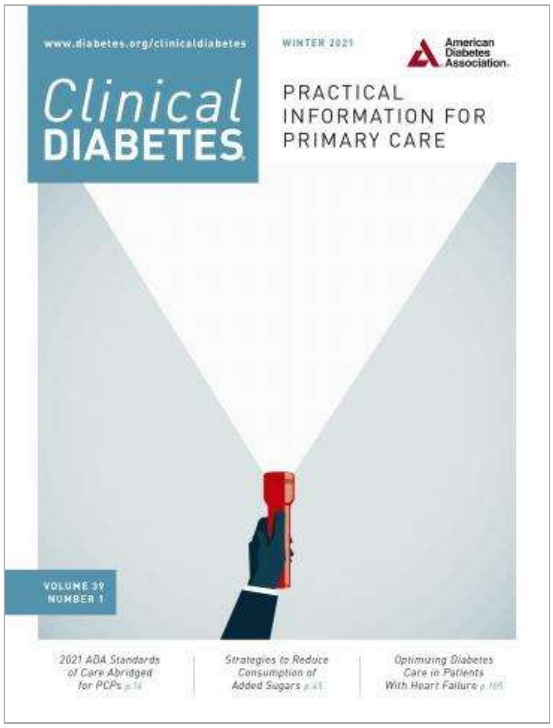


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