

# Ramosetron might be useful for treating diabetic diarrhea with a rapid small bowel transit time

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## *To the Editor,*

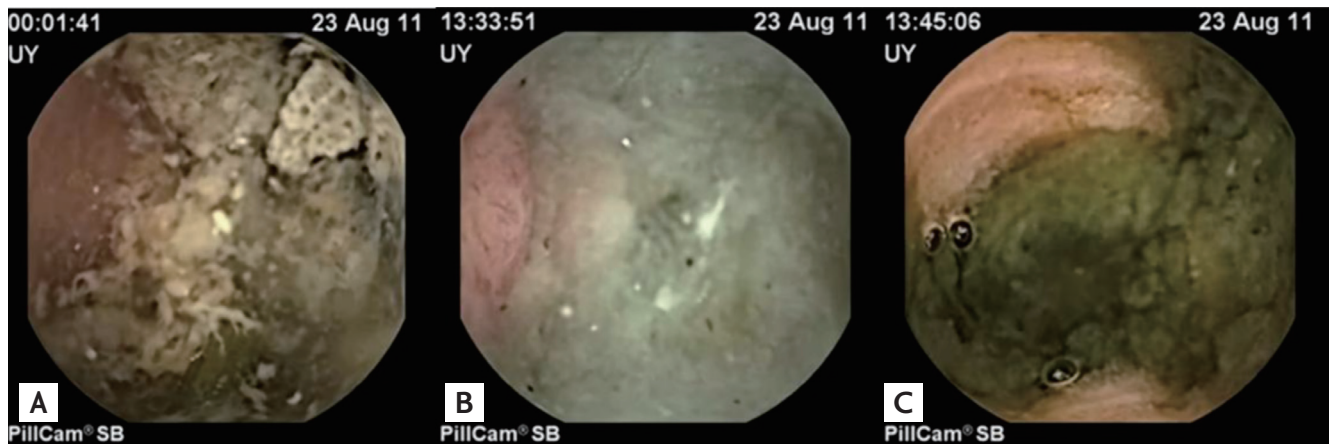
The diagnosis and treatment of diarrhea can be challenging. Diabetic diarrhea is seen mainly in patients with poorly controlled insulin-dependent diabetes who also have symptoms of diabetic peripheral and autonomic neuropathy. Typically, the diarrhea is painless, occurs during the day and night, and may be associated with fecal incontinence [1]. We used ramosetron, a selective 5-HT<sub>3</sub> receptor antagonist, to treat diabetic diarrhea with a rapid small bowel transit time.

A 49-year-old man who had developed type 2 diabetes mellitus at 42 years of age, presented with diarrhea 6 months ago. His glycemia was poorly controlled, based on a haemoglobin A<sub>1c</sub> of 17.7%. He had hypercholesterolemia, orthostatic hypotension, diabetic retinopathy, nephropathy, peripheral neuropathy, autonomic neuropathy, and gastroparesis. Current medications included insulin, losartan, atorvastatin, midodrine, metoclopramide, and domperidone. Diarrhea occurred at a frequency of > 10 bowel movements per day, with fecal urgency following meals. Steatorrhea was absent and the stool examination was unremarkable. He was prescribed conventional antidiarrheals, including a pancreatic enzyme supplement, rifaximin, probiotics, ci-

metropium bromide, and loperamide, but these were ineffective. He also had iron-deficiency anemia, as evidenced by a hemoglobin of 9.1 g/dL, mean corpuscular volume of 84.7 fL, 1.95% reticulocytes, and ferritin of 8.45 ng/mL. Capsule endoscopy (PillCam SB2, Given Imaging, Yokneam, Israel) was performed after upper endoscopy, colonoscopy, and abdominal computed tomography failed to explain the iron-deficiency anemia. He fasted for 12 hours before capsule ingestion. For 4 hours following ingestion of the capsule, only water was permitted, after which a liquid diet was offered. All medications except the losartan were discontinued. Capsule endoscopy identified multiple angiodysplastic lesions in the distal ileum. Interestingly, a markedly prolonged gastric emptying time (13 hours 33 minutes) with a rapid small bowel transit time (14 minutes) was noted (Fig. 1), suggesting gastroparesis and autonomic neuropathy, respectively. The diarrhea persisted, so ramosetron therapy (Irribow, Astellas Pharma Korea, Seoul, Korea) was started at 5 µg once daily before breakfast. The diarrhea and fecal urgency disappeared completely after 1 week of ramosetron treatment, with the bowel movement frequency reduced to two soft stools per day. On ceasing ramosetron, the diarrhea re-

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**Figure 1.** (A) Stomach. (B) Duodenum. (C) Colon. Capsule endoscopy revealed a markedly prolonged gastric transit time with rapid small bowel transit (gastric emptying time, 13 hours 33 minutes; small bowel transit time, 14 minutes).

curred, but was relieved once more when the medication was restarted. 5-Hydroxytryptamine (5-HT) acts on 5-HT<sub>3</sub> parasympathetic receptors to produce smooth muscle contraction and the release of acetylcholine from nerve terminals, causing intestinal secretion to increase [2]. The 5-HT<sub>3</sub> receptor antagonist alosetron is useful in the treatment of diarrhea in patients with irritable bowel syndrome, but must be avoided in more severe cases because of the risk of constipation [3]. The efficacy of other 5-HT<sub>3</sub> receptor antagonists such as ondansetron [4] and ramosetron [5] in the treatment of diabetic diarrhea has been documented.

In conclusion, given the inhibitory effects of a 5-HT<sub>3</sub> receptor antagonist on smooth muscle contraction and secretion, ramosetron should be considered in cases of diabetic diarrhea with rapid small bowel transit. A larger study is needed to verify the efficacy of ramosetron in treating this condition.

**Keywords:** Diabetes; Diarrhea; Ramosetron

### Conflict of interest

No potential conflict of interest relevant to this article is reported.

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