Buspirone for the Management of Functional Dyspepsia With Rapid Gastric Emptying

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ABSTRACT

Functional dyspepsia is characterized by a constellation of upper gastrointestinal symptoms consisting of epigastric pain and burning, early satiety, and postprandial fullness—all in the absence of any explanatory organic gastrointestinal pathology. Treatment options for the condition are limited, in part, because of the incomplete understanding of the pathophysiology of the disorder. A subset of patients diagnosed with functional dyspepsia are subsequently found to have rapid gastric emptying on gastric emptying scintigraphy. The significance of this finding is unknown but provides a potential therapeutic target. This case report describes functional dyspepsia with rapid gastric emptying responsive to treatment with buspirone.

INTRODUCTION

Functional dyspepsia is characterized by epigastric pain and burning, early satiety, and postprandial fullness in the absence of any known gastrointestinal pathology. Approximately 5%–10% of patients worldwide are affected by the condition, and it is responsible for up to 75% of all cases of chronic dyspepsia.1–3 Although the pathophysiology is poorly understood, several potential mechanisms have been proposed such as abnormalities in gastric compliance, visceral hypersensitivity, and postinfectious complications among others.1–3 Interestingly, a fraction of patients with functional dyspepsia are found to have rapid gastric emptying (RGE)—defined as <30% gastric retention at 1 hour on gastric emptying scintigraphy (GES).4 Whether this subset of patients is representative of a separate clinical entity is unclear because RGE is not considered in the Rome IV diagnostic criteria for functional dyspepsia.5 Regardless, RGE provides us with a potential therapeutic target for the disease. Buspirone is a 5-hydroxytryptamine 1A agonist that has been shown to augment fundic accommodation and improve postprandial symptoms in patients with functional dyspepsia.6–8

CASE REPORT

The patient is a 60-year-old man with hypertension, hyperlipidemia, chronic kidney disease Stage III, anxiety, and advanced chronic obstructive pulmonary disease status post bilateral lung transplant (on tacrolimus, mycophenolate, and prednisone). Before lung transplantation, he had undergone an esophagogastroduodenoscopy, esophageal pH testing, esophageal manometry, and a solid-phase, 4-hour GES with the only notable finding being a small hiatal hernia on endoscopy.

After lung transplantation, he transiently experienced early satiety that resolved within a few days (GES was unremarkable). Several months later, the patient developed heartburn and regurgitation and presented to gastroenterology clinic. Esophageal manometry demonstrated hypercontractile peristalsis in all swallows while esophageal pH testing, performed after 7 days off a proton pump inhibitor (PPI), demonstrated increased esophageal acid exposure with percentage acid exposure times consisting of 12.8% (upright), 7.1% (supine), and 9.2% (total) with a DeMeester score of 33.5. The patient was prescribed pantoprazole 40 mg once daily and encouraged to try a sleep positioning device (MedCline pillow) to facilitate left lateral positioning and minimize nightly reflux. Repeat pH testing a few months later (while off PPIs for 7 days) demonstrated a resolution of his acid reflux with percentage acid exposure times being 0.5% (upright), 2.4% (supine), and 2.1% (total) with a DeMeester score of 9.3.
Two years after lung transplantation, he began experiencing persistent epigastric discomfort, severe nausea with vomiting, early satiety, and loose stools culminating in 5 hospitalizations over a 1-year period. A workup consisting of stool studies (Clostridiodes difficile assay, stool cultures, and ova/parasites), urine toxicology, abdominal computed tomography, esophagogastroduodenoscopy (normal gastric biopsies negative for Helicobacter pylori), and colonoscopy were all unremarkable.

The patient returned to gastroenterology clinic and underwent a solid-phase GES that revealed 93% emptying at 1 hour which is consistent with RGE. The patient was diagnosed with functional dyspepsia with evidence of RGE and started on buspirone 10 mg 3 times daily (30 minutes before meals). Within 1 week of starting the buspirone, he reported complete resolution of his nausea with vomiting, early satiety, and diarrhea.

DISCUSSION

Functional dyspepsia is a chronic disorder with persistence of symptoms occurring in up to 50% of patients.1 Current guidelines recommend a stepwise approach to management: first-line therapy being a 4–8 week trial of a PPI and second-line therapy involving the use of a tricyclic antidepressant (usually amitriptyline).9 Although treatment with PPIs and/or tricyclic antidepressants provides relief for some, a significant number of individuals complain of refractory symptoms.10 The options for managing refractory functional dyspepsia are limited—consisting of a trial of a prokinetic agent or psychological therapy.1,2 Interestingly, a fraction of patients with functional dyspepsia have RGE on GES.3 Classically, RGE lies within the spectrum of functional dyspepsia, although recent work suggests that it may be its own distinct condition.4 Regardless, RGE provides us with an additional therapeutic target.

Buspirone was first synthesized in 1968 for its presumed antipsychotic properties.11 Today, it is primarily used in the treatment of generalized anxiety disorder in patients who fail therapy with a selective serotonin reuptake inhibitor or develop intolerances to selective serotonin reuptake inhibitors.11 However, in addition to anxiolysis, buspirone has been shown to promote fundic relaxation and increase gastric accommodation by acting as an agonist of gastric 5-hydroxytryptamine 1A receptors.12,13

The fundus of the stomach plays a crucial role in facilitating gastric accommodation in response to a meal. Interestingly, up to 50% of patients with functional dyspepsia have impaired gastric accommodation.7 Physiologically, impairments in gastric accommodation may result in early redistribution of a meal to the distal stomach, where it can produce RGE.7 Based on this premise, using buspirone to promote fundic relaxation and accommodation may be of benefit in patients with functional dyspepsia who are found to have RGE.

A few studies have evaluated the use of buspirone in patients with functional dyspepsia. Tack et al found that 4 weeks of buspirone led to a significant improvement in gastric accommodation, gastric emptying of liquids, and dyspeptic symptoms in patients with functional dyspepsia.9 Similarly, Caviglia et al found that patients treated with buspirone over a 3-month period had a significant reduction in the rate of gastric emptying and an improvement in dyspeptic symptoms (particularly early satiety).7 It appears that buspirone doses higher than 20 mg daily may slow the rate of gastric emptying, whereas daily doses greater than 30 mg promote fundic relaxation and increase proximal stomach volume.9 In addition, a significant benefit of buspirone is its minimal side effect profile—with the only major side effect being dizziness (seen in fewer than 10% of patients).11

In conclusion, buspirone may mediate the alleviation of symptoms secondary to RGE in patients with functional dyspepsia. Where available, buspirone may be an effective, safe, and well-tolerated therapeutic option in this particular patient population. Further research of patients with functional dyspepsia and RGE will hopefully help delineate whether these are 2 distinct conditions or variants of the same disorder.

DISCLOSURES

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