New Causes for the Old Problem of Bile Reflux Gastritis

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Grant support: none

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Disclosures: Neither author has any conflicts of interest to disclose.

Writing Assistance: The authors acknowledge Tom Emmett, MD, MLS, for his contributions to the literature search.

Author contributions: Both authors contributed to the planning, drafting, and critical revision of the manuscript.

Bile reflux gastritis

Introduction.

Bile reflux gastritis (also known as "duodenogastric reflux," "biliary gastritis," or "alkaline reflux gastritis") occurs when there is retrograde movement of bile into the stomach, leading to clinical symptoms, endoscopic changes, and histologic features of a chemical (reactive) gastritis. While William Beaumont first observed bile reflux in a patient with a gastrocutaneous fistula in 1833[1], it was not until gastric surgery became routine in the late 1800s that the clinical importance of this problem was recognized. For nearly a century, this was thought to be a surgical disease, caused by resection or alteration of the pylorus. However, bile reflux gastritis is increasingly found in individuals without prior gastric surgery, a problem termed "primary biliary reflux." Both surgical and pharmacologic interventions are used to treat this challenging condition.

Description of the clinical problem

Bile reflux gastritis can result from excess bile in the duodenum, lack of a pylorus as a barrier to retrograde flow, and/or decreased anterograde peristalsis of the stomach and duodenum. (See Figure 1) This can occur following gastric or biliary surgery or as primary biliary reflux. The most common predisposing surgeries are those that either remove, disrupt or bypass the pylorus, resulting in unopposed reflux of duodenal contents.

Primary biliary reflux occurs in the absence of gastric surgery. Risk factors include gallbladder dysfunction and gastric or duodenal dysmotility.[2] Cholecystectomy predisposes to bile reflux due to loss of the gallbladder as a bile reservoir.[3] Biliary sphincterotomy leads to increased flow of bile through the sphincter of Oddi. Phase III of gastroduodenal motility (the migratory motor

complex) plays an important role, both in preventing duodenogastric reflux and in clearing the antral region of refluxed material. Individuals with bile reflux gastritis have been shown to have a decreased frequency of migratory motor complexes, suggesting that the gastritis might be related to a prolonged mucosal exposure to bile.[7]

Recurrent and excessive exposure of gastric mucosa to bile reflux can lead to both endoscopic and histologic changes with or without symptoms. Evidence for this has been elegantly reviewed elsewhere.[4] Symptoms are vague and variable, but they can include abdominal pain, dyspepsia, nausea with bilious vomiting, weight loss or heartburn. Although the prevalence of bile reflux gastritis is unknown, the use of opioid pain medications, prevalence of type II diabetes mellitus, and performance of intestinal transplant surgeries are increasing, and all can be associated with gastroduodenal dysmotility.

Diagnosis

The diagnosis of bile reflux gastritis can be challenging, particularly in those without surgical risk factors. Endoscopic and histologic findings may be non-specific, or not well recognized by clinicians. Although there are no universally accepted criteria, it is generally felt that evidence of duodenogastric reflux in conjunction with histologic changes of gastritis is sufficient to make the diagnosis. Modalities for establishing bile reflux include visualization of duodenogastric reflux or bile pooling in the stomach on endoscopy (see Figures 2 and 3), detection of bile salts in gastric fluid, measurement of bilirubin in the stomach using a fiber optic spectrophotometer or biliary radionuclide scanning showing radiotracer in the stomach; the latter three are not routinely performed in clinical practice.[5, 6] Endoscopic findings most often include erythema of

the gastric mucosa and the presence of bile in the stomach (see Figure 4); thickened gastric folds, erosions, and gastric atrophy can also be seen.[3, 7] Histologic examination shows features of a chemical gastritis including foveolar hyperplasia, edema, smooth muscle fibers in the lamina propria and paucity of acute or chronic inflammatory cells.[8, 9] These features are similar to those seen in chronic non-steroidal anti-inflammatory drug use and other chemical injuries, so it is important to exclude this competing etiology.

Management

Management of bile reflux gastritis includes both medical and surgical options. Several medical therapies have been evaluated in uncontrolled or small controlled trials with variable results. Proton pump inhibitors are commonly used, although the mechanism of action is not clear. Bile acids are thought to cause damage due to their detergent properties; however, most precipitate at a low pH and cause more damage to gastric mucosa at a higher pH.[4] A randomized trial involving 60 post-cholecystectomy patients compared sucralfate (2 g twice daily) versus rabeprazole (20 mg daily) or no treatment.[10] In this study, epigastric pain was reduced by 45% in patients on sucralfate, by 30% in patients on rabeprazole and by 10% in the control group. Heartburn was reduced by 44% in the sucralfate group, 35% in the rabeprazole group and 15% in the control group. Endoscopic scores decreased in the treatment groups, although it was not clear whether the endoscopists were blinded. Another controlled trial for sucralfate found histologic but not symptomatic improvement. Ursodeoxycholic acid (UDCA) (1000 mg/day) was studied in a cohort of 11 patients with prior gastric surgery[11]. During treatment, the bile acid content in the stomach had a demonstrable change to UDCA. Five patients were treated for four weeks with placebo followed by four weeks of UDCA; these patients had no change in

symptoms with placebo but did improve after 4 weeks of UDCA. An additional seven patients were treated with UDCA followed by placebo; they had improvements on therapy but only 3 had recurrence of symptoms after the placebo period. Neither endoscopic appearance nor histology changed. Cholestyramine combined with alginates and Prostaglandin E2 have also been studied in small controlled trials but were ineffective. The role of pro-kinetic agents in the management of bile reflux gastritis has not been well studied. The goal of treatment is to relieve symptoms; although an increased risk of gastric adenocarcinoma has been theorized and suggested by animal models, this risk has not been demonstrated in humans.

Surgical management of bile reflux aims to divert bile away from the stomach. These procedures are reserved for only severely symptomatic patients, generally where the reflux is caused by prior surgery. The most commonly utilized procedures include interposed isoperistaltic jejunal (Henley) loop, Braun enteroenterostomy and a roux-en-Y procedure. A roux-en-y choledochojejunostomy can be used to divert bile directly from the biliary tree after cholecystectomy.[5] These procedures are effective in relieving symptoms but can be complicated by stomal ulcerations, roux stasis syndrome, and bezoar formation.

As a general treatment approach, the first step may be to stop any nonessential medications that might reduce gastroduodenal motility (see Figure 5). If medical therapy is necessary, given the lack of strong evidence for any particular therapy, we believe it is reasonable to start with a proton pump inhibitor. This is part of the treatment algorithm for dyspepsia, and it may treat etiologies of symptoms beyond bile reflux gastritis. If this is ineffective, ursodeoxycholic acid 300mg three times daily may be tried. If symptomst persist, sucralfate 1-2g twice daily or a

proton pump inhibitor may be the next option. Combination therapy could be tried if individual therapies are ineffective. Finally, for severely symptomatic patients, particularly those whose reflux is caused by prior surgery, surgical diversion of bile can be considered.

Take-home messages

- Bile reflux gastritis is a well-known complication of gastric surgery, particularly those that disrupt or bypass the pylorus.
- Primary biliary reflux is a more recently recognized problem that occurs in patients without gastric surgery and is related to excess bile in the duodenum (due to cholecystectomy, gallbladder dysmotility or sphincterotomy) or decreased gastric or duodenal motility.
- The diagnosis of bile reflux gastritis requires recognizing risk factors in symptomatic patients, followed by confirming the presence of bile in the stomach along with characteristic histologic findings.
- As the prevalence of conditions that alter gastrointestinal motility continues to increase, it is important that clinicians suspect and recognize this diagnosis.
- Treatment can be challenging but often includes a trial of medical therapy that may include ursodeoxycholic acid, sucralfate, or proton pump inhibitors.
- Patients with bile reflux gastritis related to prior surgery may benefit from surgical diversion of bile if medical treatments fail.

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Figure Legends.

Figure 1 – Factors that can contribute to bile reflux gastritis. Gallbladder dyskinesia or surgical removal of the gallbladder lead to loss of the normal reservoir for storing bile. Sphincterotomy removes the barrier to bile flow into the duodenum. Surgical resection or alteration of the pylorus, such as in Billroth I or II or pyloroplasty, removes the barrier for retrograde bile flow into the stomach. Dysmotility of the stomach or duodenum can lead to retrograde movement or stasis of bile.

Bile reflux gastritis

Figure 2

Bile pooling in the stomach in a patient with a Billroth 1 anastomosis

Bile reflux gastritis

Figure 3

Bile pooling in the stomach of a patient without previous gastric surgery

Bile reflux gastritis

Figure 4

Striped erythema in a patient with bile reflux gastritis

Figure 5

Proposed treatment algorithm

Bile reflux gastritis