MINDFUL PRACTICE

Nonsurgical Management of Anal Fissures

BY JON O. EBBERT, M.D., AND ERIC G. TANGALOS, M.D.

The Problem

A 32-year-old woman with a history of fibromyalgia and irritable bowel syndrome presents for evaluation of rectal pain of 3 weeks' duration. She has had episodes of diarrhea alternating with constipation for years. Despite psyllium therapy, her stools have been hard and difficult to pass. During defecation 3 weeks ago, she developed excruciating pain that lasted for 60 minutes. She says it feels like she is passing "broken glass" with every bowel movement. She has noted occasional blood on the toilet paper. She denies constitutional symptoms, and is afebrile with normal vital signs. On exam, she has pain with light touch all over her body and reports a diffusely tender abdomen with no rebound or guarding. Rectal exam reveals tenderness at the 12 o'clock position with evidence of a superficial ulcer. You diagnose an anal fissure and consider conservative topical therapy as a first approach. You wonder about recent evidence supporting the use of topical agents to treat pain and promote healing of anal fissures.

The Question

In patients with an anal fissure, which nonsurgical interventions are superior to placebo for promoting healing and decreasing time to resolution of pain?

The Search

You open PubMed (www.pubmed.gov), enter "anal fissures," and limit the search to meta-analysis. You find a relevant study. (See box at right.)

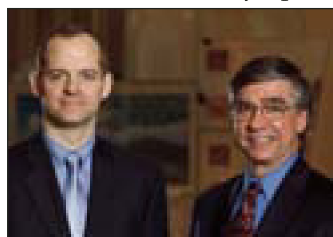
Our Critique

The absence of an effect of lidocaine confirms conventional wisdom that pain relief alone is not sufficient to heal anal fissures. Medical therapy traditionally consists of relief of sphincter hypertonia, maintenance of atraumatic passage of stool (i.e., increased fiber intake), and pain relief. Sphincterotomy was superior to pharmacologic therapy, with the caveat that it may increase the risk for fecal incontinence. However, the author concluded that incontinence rates with surgery were equal to those with nitroglycerin and botulinum toxin type A (Botox) but perhaps less than with calcium channel blockers. Although fecal incontinence with topical pharmacotherapies is reversible, that is not the case with a surgical intervention. Nitroglycerin applied as a patch distal to the anus was as effective as nitroglycerin applied to the anus. For patients who may have difficulty with clinical application, a patch could be considered but should be started at the lowest possible dose to avoid headaches. If headaches develop with nitroglycerin, patients should use fewer applications per day. Hydrocortisone should be applied only to anal fissures with an inflammatory component, or healing may be inhibited. The author notes that despite the 95% cure rate with surgery (e.g., sphincterotomy), medical therapy is successful in most patients and surgery should be reserved for refractory cases.

Clinical Decision

You prescribe 0.3% nitroglycerin in plastibase to be applied to the anus twice per day. She reports that her pain significantly improved but recurred with discontinuation of therapy. You repeat treatment but consider sphincterotomy in the future.

DR. EBBERT *and* DR. TANGALOS *are with the Mayo Clinic in Rochester, Minn. They report having no conflicts of interest. To respond to this column or suggest topics for consideration, write to Dr. Ebbert and Dr. Tangalos at our editorial offices or e-mail them at imnews@elsevier.com.*



R.L. Nelson.

Non surgical therapy for anal fissure. Cochrane Database Syst. Rev. 2006;(4):CD003431.

► **Criteria for study inclusion:** Participants were randomized to nonsurgical therapy for anal fissures. Comparison groups included operative procedures, other medical therapy, or placebo.

► **Subjects:** Studies included participants with chronic anal fissures (lasting more than 4 weeks), or with pain of less duration but with similar past episodes. Chronicity may be suggested by sentinel pile at the distal fissure margin, heaped-up fissure edges, visible sphincter fibers at fissure base, or an inflammatory polyp at the inner fissure margin.

► **Outcomes:** The primary outcomes were fissure persistence (i.e., pain) and post-therapy minor incontinence. Data on adverse events were also collected.

► **Study identification:** The author searched PubMed from 1966 to May 2006 as well as the references of retrieved studies, the Cochrane Library, the Cochrane Colorectal Cancer Group, and EMBASE. Authors were queried about unpublished ongoing studies.

► **Results:** A total of 54 randomized, controlled clinical trials of adults and children were included. Pharmacologic agents used included nitroglycerin ointment, isosorbide dinitrate, Botox, diltiazem, nifedipine, hydrocortisone, lidocaine, bran, indoramin (antiadrenergic agent), and minoxidil. Nitroglycerin ointment significantly decreased the odds of nonhealing (i.e., persistence or recurrence), compared with placebo. Nitroglycerin was no worse than Botox or calcium channel blockers, and was significantly better than lidocaine. The dose of nitroglycerin did not make a difference. Headache was the most common adverse effect with this agent, compared with placebo), occurring in 27% of patients. Calcium channel blockers (diltiazem and nifedipine) given orally or topically were not significantly more effective than nitroglycerin, but were less likely than nitroglycerin to cause headache. Neither indoramin nor minoxidil were effective for healing anal fissures. Bran decreased the risk for acute fissure recurrence, compared with placebo. Interestingly, the combined healing rate in the placebo patients was 34%.

Immunoassay Might Aid Early Detection Of Pancreatic Cancer

BY KERRI WACHTER

An investigational monoclonal antibody can be used to identify early-stage pancreatic cancer, researchers reported.

"We were able to identify the overwhelming majority of patients with early-stage disease," lead author David V. Gold, Ph.D., said in a teleconference in advance of presentation of the findings at the American Society of Clinical Oncology's annual gastrointestinal cancer symposium. The PAM4 monoclonal antibody (clivatuzumab) quantifies blood levels of the PAM4 protein "that appears to be relatively unique to pancreatic cancer," he said.

The researchers analyzed data on about 68 patients who had undergone surgery for pancreatic cancer, and 19 healthy controls. The sensitivity of the PAM4 blood test for detecting stage I pancreatic cancer (disease confined to the pancreas), stage II disease (disease that has spread to nearby organs), and stage III/IV cancers (disease with local and distant spread) was 62%, 86%, and 91%, respectively. Overall, the assay was 81% sensitive for detecting pancreatic cancer.

The PAM4 antibody also has the potential to be part of an effective therapy. "Detection of the PAM4 antigen in the blood of these patients means that the cancer is producing the protein, and that this protein may act as a marker on the tumor for use of the antibody to target drugs and/or radioisotopes directly to the tumor," said Dr. Gold, a researcher at the Garden State Cancer Center in Belleville, N.J.

Researchers have begun to explore attaching radioisotopes to the antibody in order to image tumors, or to target radiotherapy in combination with chemotherapy. In a small related study, the researchers achieved a partial response rate (defined as at least a 30% reduction in the size of the tumor) of 23% and a stable disease rate of 45% in patients with stage III and IV pancreatic cancer.

Dr. Gold estimated that the assay and related therapies are 2-3 years from clinical use. ■

Disclosures: *Senior author Dr. David Goldenberg is the chief scientific officer and chairman of the board of directors for Immunomedics, which develops monoclonal antibody–based treatments. Dr. Gold did not provide a disclosure statement.*

MY TAKE

Hope for Earlier Diagnosis

Early diagnosis of pancreatic cancer can lead to a 10-fold improvement of survival (about 20% 5-year surgical survival for stage I disease versus 2% for stage IV disease). The problem has always been how to identify the patient with early disease.

The recent discovery that circulating blood levels of PAM4 (quantified through use of the monoclonal antibody clivatuzumab) are "relatively unique to pancreatic cancer" and positive in 68% of those with stage I pancreatic cancer raises hopes that we will have a tool for earlier diagnosis.

We need to know more about the protein and the false-positive rates, to ensure that it is not prevalent in noncancer patients with chronic pancreatitis, diabetes mellitus, cigarette smoking, and other conditions that predispose to pancreatic cancer. That information and the development of an algorithm for assessing circulating levels of PAM4 as a screening test will be important to determining its future clinical use.

ROWEN K. ZETTERMAN, M.D., *a gastroenterologist, is dean of the school of medicine at Creighton University, Omaha, Neb. He reported no conflicts of interest.*