

# RECENT ADVANCES IN THE PHARMACOTHERAPY OF ACUTE & CHRONIC ANAL FISSURE



## WHAT CAUSES ANAL FISSURES?

Anal fissures are caused by trauma to the anus and anal canal. The cause of the trauma usually is a bowel movement, and many people can remember the exact bowel movement during which their pain began. The fissure may be caused by a hard stool or repeated episodes of diarrhea. Occasionally, the insertion of a rectal thermometer, enema tip, endoscope, or ultrasound probe (for examining the prostate gland) can result in sufficient trauma to produce a fissure. During childbirth, trauma to the perineum (the skin between the posterior vagina and the anus) may cause a tear that extends into the anoderm. The most common location for an anal fissure in both men and women (90% of all fissures) is the midline posteriorly in the anal canal, the part of the anus nearest the spine. Fissures are more common posteriorly because of the configuration of the muscle that surrounds the anus. When fissures occur in locations other than the midline posteriorly or anteriorly, they should raise the suspicion that a problem other than trauma is the cause. Other causes of fissures are anal cancer, Crohn's disease, leukemia as well as many infectious diseases including tuberculosis, viral infections (cytomegalovirus or herpes), syphilis, gonorrhea, Chlamydia, chancroid (Hemophilus ducreyi), and human immunodeficiency virus (HIV). Among patients with Crohn's disease, 4% will have an anal fissure as the first manifestation of their Crohn's disease, and 50% of all patients with Crohn's disease eventually will develop an anal ulceration that may look like a fissure. Studies of the anal canal in patients with anal fissures consistently show that the muscles surrounding the anal canal are contracting too strongly (they are in spasm), thereby generating a pressure in the canal that is abnormally high.

The supply of blood to the anus and anal canal also may play a role in the poor healing of anal fissures. Ultrasound studies that measure blood flow showed that the posterior anal canal had less than half of the blood flow of other parts of the canal. This relatively poor flow of blood may be a factor in preventing fissures from healing. It also is possible that the increased pressure in the anal canal due to spasm of the internal anal sphincter may compress the blood vessels of the anal canal and further reduce the flow of blood.

## WHAT ARE THE SYMPTOMS OF ANAL FISSURES?

People with anal fissures almost always experience anal pain that worsens with bowel movements. The pain following a bowel movement may be brief or long lasting; however, the pain usually subsides between bowel movements. The pain can be so severe that patients are unwilling to have a bowel movement, resulting in constipation and even fecal impaction. Moreover, constipation can result in the passage of a larger, harder stool that causes further trauma and makes the fissure worse. The pain also can affect urination by causing discomfort when urinating (dysuria), frequent urination, or the inability to urinate. Bleeding in small amounts, itching (pruritus ani), and a malodorous discharge may occur due to the discharge of pus from the fissure. As previously mentioned, anal fissures commonly bleed in infants.

## WHAT IS THE TREATMENT FOR ANAL FISSURES?

The goal of treatment for anal fissures is to break the cycle of spasm of the anal sphincter and its repeated tearing of the anoderm.

## GENERAL TREATMENT AND HOME REMEDIES FOR ANAL FISSURES

In acute fissures, medical (non-operative) therapy is successful in the majority of patients. Of acute fissures, 80% to 90% will heal with conservative measures as compared with chronic (recurrent) fissures, which show only a 40% rate of healing.



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Initial treatment involves adding bulk to the stool and softening the stool with psyllium or methylcellulose preparations and a high fiber diet. Other home remedies may include avoiding "sharp" foods that may not be well-digested (i.e., nuts, popcorn, tortilla chips), increasing liquid intake, and, at times, take stool softeners (docusate or mineral oil preparations).

## PRESCRIPTION MEDICATIONS FOR ANAL FISSURES

### ANESTHETICS AND STEROIDS

Topical anesthetics (for example, xylocaine, lidocaine, tetracaine, pramoxine) are recommended especially prior to a bowel movement to reduce the pain of defecation. Often, a small amount of a steroid is combined in the anesthetic cream to reduce inflammation. The use of steroids should be limited to two weeks because longer use will result in thinning of the anoderm (atrophy), which makes it more susceptible to trauma. Oral medications to relax the smooth muscle of the internal sphincter have not been shown to aid healing.

### NITROGLYCERIN

Because of the possibility that spasm of the internal sphincter and reduced flow of blood to the sphincter play roles in the formation and healing of anal fissures, ointments with the muscle relaxant, nitroglycerin (glyceryl trinitrate), have been tried and found to be effective in healing anal fissures. Nitroglycerin has been shown to cause relaxation of the internal anal sphincter and to decrease the anal resting pressure. When ointments containing nitroglycerin are applied to the anal canal, the nitroglycerin diffuses across the anoderm and relaxes the internal sphincter and reduces the pressure in the anal canal. This relieves spasm of the muscle and also may increase the flow of blood, both of which promote healing of fissures. Unlike Nitropaste, a 2.0% concentration of nitroglycerin that is used on the skin for patients with heart disease and angina, the nitroglycerin ointment used for treating anal fissures is pharmaceutically compounded into a concentration of nitroglycerin of only 0.2%. One randomized, controlled trial has demonstrated the healing of anal fissures in 68% of patients with nitroglycerin as compared to 8% of patients treated with placebo (inactive treatment). Other studies have shown a 33% to 47% recurrence rate of fissures following treatment with nitroglycerin. The presence of a sentinel pile is associated with a lower healing rate with nitroglycerin treatment. The dose of nitroglycerin often is limited by side effects. The usual side effects are headache (due to dilation of blood vessels in the head) or light-headedness (due to a drop in blood pressure). This type of formulation may be applied using a small amount of ointment be applied to a cotton-tipped swab with the swab then inserted into the anus only for the depth of the cotton-tipped portion of the swab. Ointment smeared only around the outside of the anus does not reach the anoderm where its effects are important, yet the nitroglycerin will be absorbed and produce side effects. Nitroglycerin is more rapidly absorbed if blood flow in the anoderm is high. For this reason, it is recommended that nitroglycerin not be applied within 30 minutes of a bath since the warm water of the bath enlarges (dilates) the blood vessels in the skin and anoderm and increases their flow of blood. Additionally, the first application of nitroglycerin should be at bedtime while the patient is lying down in order to prevent falls due to light-headedness.

### CALCIUM CHANNEL BLOCKING DRUGS (CCBS)

As is the case with nitroglycerin, ointments containing calcium channel blocking drugs (for example, nifedipine or diltiazem) relax the muscles of the internal sphincter. They also expand the blood vessels of the anoderm and increase the flow of blood. Nifedipine ointment (2%) is applied in a manner similar to nitroglycerin ointment, but seems to produce fewer side effects. Although healing of chronic fissures has been reported in up to 67% of patients treated with calcium channel blockers, they are most effective with acute fissures.

### TOPICAL NIFEDIPINE WITH LIDOCAINE IN ADULTS

Chronic anal fissure may be treated by chemical or surgical sphincterotomy. Perrotti et al were testing the efficacy of local application of nifedipine and lidocaine ointment in healing chronic anal fissure. The study was a prospective, randomized, double-blind design.

The patients were divided into two groups nifedipine group (n = 55) used topical 0.3% nifedipine and 1.5 % lidocaine ointment every 12 hours for 6 weeks, and a control group (n = 55) received topical 1.5 % lidocaine and 1 % hydrocortisone acetate ointment during therapy. Healing of chronic anal fissure was achieved after 6 weeks of therapy in 94.5% of the nifedipine-treated patients (P < 0.001) as opposed to 16.4 percent of the controls. No systemic side effects in patients treated with nifedipine were detected. They concluded that the study clearly demonstrates that the therapeutic use of topical nifedipine and lidocaine ointment should be extended to the conservative treatment of chronic anal fissure.

### TOPICAL NIFEDIPINE WITH LIDOCAINE IN CHILDREN

Klin et al evaluated the safety and efficacy of using nifedipine gel with lidocaine in treatment of acute anal fissures in children by reviewing the cases of 106 children with acute anal fissure treated conservatively by nifedipine gel with lidocaine between the years 2003-2012. The retrospective analysis included 48 male and 58 female patients with clinical presentations consisting of constipation, rectal bleeding, anal pain, perianal itching, abdominal pain, irritability and rectal prolapse. Posterior, anterior, both anterior and posterior, multiple, both posterior and lateral locations were the main physical findings in 65, 23, 10, 7, and 1 cases, respectively. Ninety-nine patients completed the 4-week treatment course of nifedipine gel with lidocaine successfully (93.40%), with complete healing of the fissure. The recurrence rate observed was very low (6.60%). The authors concluded that topical 0.2% nifedipine with lidocaine appears an efficient mode of treatment for anal fissures in children, with a significant healing rate and no side effects.

### BOTULINUM TOXIN

Botulinum toxin (Botox) relaxes (actually paralyzes) muscles by preventing the release of acetylcholine from the nerves that normally causes muscle cells to contract. It has been used successfully to treat a variety of disorders in which there is spasm of muscles, including anal fissures. The toxin is injected into the external sphincter, the internal sphincter, the intersphincteric groove (an indentation just inside the anus that demarcates the dividing line between external and internal sphincters), or into the fissure itself. The dose is not standardized and has varied from 2.5 to 20 units of toxin in two locations (usually on either side of the fissure). The cost of a 100 unit vial of toxin is several hundred dollars and unused toxin cannot be saved. Thus, the expense for a single injection of toxin is high. One representative study found that fissures healed in 87% of patients by six months after treatment with botulinum toxin. By 12 months, however, the healing rate had fallen to 75% and by 42 months to 60%. The primary side effect of botulinum toxin is weakness of the sphincters with varying degrees of incontinence (leakage of stool) that usually is transient. Other side effects are not common. There is also a great variability in the medical literature with respect to the effectiveness of drugs and botulinum toxin in the healing of anal fissures. Healing may be temporary and fissures may return with a hard bowel movement. When patients are intolerant or unresponsive to non-surgical treatments, surgery becomes necessary.

**After reading this article,  
would you like to start a  
prescription for a patient?**

If so, please call, write, or fax in the following prescription:

**Adults**  
Nifedipine/Lidocaine 0.3%/1.5% Ointment 60gm  
Apply every 12 hours for 6 weeks

**Children**  
Nifedipine/Lidocaine 0.2/1.5% Ointment 30gm  
Apply every 12 hours for 4 weeks

**Phone: (949) 642-0106**  
**fax: (949) 642-5039**