Anal Fissure

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ABSTRACT

Anal fissure is a common problem, vexing to both patients and physicians. The historical mainstay of therapy has been some method of partial division of the internal anal sphincter with the serious potential complication of fecal incontinence. Nonsurgical treatment methods were therefore pursued, producing healing rates less than that seen after surgical therapy but none of the morbidity of surgery. This article summarizes accepted methods of modern medical and surgical therapy for anal fissure and offers a rationale for treatment type selection.

KEYWORDS: Anal fissure, sphincterotomy, anal pain

Objectives: On completion of this article, the reader should be able to summarize the current management of anal fissure.

An anal fissure* is a crack or tear in the vertical axis of the squamous lining of the anal canal between the anal verge and the dentate line. The classic symptom is pain during and following defecation, lasting minutes to hours. Bright red bleeding is common, most often seen on the toilet tissue and occasionally streaked onto the stool itself. Fissures occur most often in the posterior midline in both men and women, although anterior midline fissures are more commonly seen in women. Acute fissures are superficial but may deepen to expose the underlying internal sphincter. Chronic fissures are associated with secondary changes, which may include a sentinel tag, hypertrophied anal papilla, induration of the edge of the fissure, and/or relative anal stenosis secondary to spasm or fibrosis of the internal sphincter.

Efforts should be made to identify the precipitating cause of the individual patient's fissure (such as constipation or diarrhea) and manage it appropriately; otherwise, the likelihood of recurrence is high. In a minority of patients, a fissure may be associated with a systemic disease (e.g., Crohn's disease) or may be attributable to another diagnosis (e.g., anal carcinoma, sexually transmitted disease). In these cases, treatment of the underlying pathology is a top priority.

PATHOGENESIS

Fissures are usually caused by local trauma to the anal canal, typically overstretching of the anoderm by a hard, nondeformable stool. However, other forms of forceful stretching, as well as repeated episodes of loose diarrheic stool, may also precipitate a fissure. Several anatomic and dynamic studies support the hypothesis that relative ischemia of the posterior midline anal canal contributes to poor healing. Internal sphincter hypertonicity has also been implicated as a pathologic finding, but whether this is cause or effect remains unclear. Treatment that is successful in producing fissure healing also demonstrates an increase in anodermal blood flow.

**As this is intended to be a clinical update, emphasis is on newer treatment information. Older supporting references that can be found in standard texts have been omitted here.*

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Investigation has also revealed abnormalities at the cellular level. An observed increase in neural proliferation in chronic fissures has been postulated as contributory to the pain of both fissure and pruritis.[1] In another study, patients with fissures and hemorrhoids were shown to have circulating anti–endothelial cell antibodies, leading the authors to hypothesize that the interaction of immune components with anal canal endothelium could contribute to ischemia and hypertonicity.[2]

TREATMENT

The Basics

Increased fluid and fiber ingestion, use of sitz baths for pain relief, and use of stool softeners such as docusate sodium or docusate calcium are very safe, have virtually no side effects, often decrease pain and bleeding, and should be instituted as a first step for patients with fissure. Healing occurs in up to 50% of patients when so treated. Use of topical anesthetics does not decrease healing rates and is safe, with a low incidence of sensitivity to the agent or vehicle. Maintaining appropriate fluid and fiber intake can minimize recurrence. Local application of heat has been shown to relax the hypertonic anal sphincter. However, care must be taken to avoid potentially serious burns to the perianal and gluteal areas.[3]

Nonsurgical Therapy

A Cochrane review of fissure treatment[4] concluded that topical and injected therapies are marginally better than placebo in healing fissures and recommended lateral internal sphincterotomy (LIS) as the "gold standard" for anal fissure. Nevertheless, these agents remain in widespread use. There are several possible reasons for this. One may be reluctance on the part of many patients and surgeons to proceed immediately to sphincterotomy in the presence of increasing evidence that impaired continence after sphincterotomy is more common than previously thought.[5–8] Nonsurgical therapy also has other advantages, including low risk, repeatability, and the possibility of using a combination of agents to produce improved results.[9–11] One should also remember that LIS requires surgical expertise and operating room time to perform, thus increasing the usage of increasingly scarce health care resources.

NITRIC OXIDE DONORS

Nitric oxide (NO) is the predominant neurotransmitter mediating relaxation of the human internal anal sphincter.[12] Nitric oxide donors probably promote healing by lowering intra-anal pressure, thereby increasing local blood flow. NO donors may also vasodilate blood vessels supplying the anal canal.[13] Several different NO donors are currently in use worldwide.

Topical nitroglycerin ointment is the treatment most commonly used for nonsurgical therapy of anal fissure in the United States. Several strengths have been evaluated, and of these, 0.2% appears to provide the best balance between desired effect (lowering anal resting pressure by up to 33%) and side effects, principally headache. Higher concentrations do not appear to have a therapeutic advantage, and side effects are significantly increased.

In conjunction with counseling regarding appropriate fluid and fiber intake, patients are instructed to apply the topical nitroglycerin ointment up to three times daily. Most patients report pain relief very soon after starting therapy with topical nitroglycerin, which is an advantage. The most common side effect, a dose-related headache, causes less than one patient in five to stop therapy. The efficacy of topical nitroglycerin in healing anal fissures is variable. Healing rates have been reported as high as 67%, and symptom-free rates are as high as 75%.[14] The need for repeated applications has been cited by some authors as a drawback of therapy, but that has not been a complaint of most patients. However, a multicenter, double-blinded randomized controlled trial of topical nitroglycerin versus placebo showed no effect of topical nitroglycerin on healing of anal fissures, but it did decrease pain.[15] As a result of this study, Food and Drug Administration approval for topical nitroglycerin ointment was denied, and there is as yet no commercially manufactured preparation in the United States, requiring that the ointment be compounded in a pharmacy with possible variations in quality control.

In a small randomized study, the use of a 10-mg transdermal nitroglycerin patch was equivalent to 0.2% nitroglycerin topical ointment in relief of pain and fissure healing.[16] The patch was applied on the flank below the level of the umbilicus for 24 hours and changed daily. The authors noted that the patch offered better compliance and patient acceptability; however, this is not being clinically employed at present.

Patients who fail to heal with nitroglycerin, or who cannot tolerate nitroglycerin's side effects, can be subsequently treated with other agents, such as topical diltiazem[9] (see later), topical L-arginine[17] (an intrinsic precursor of nitric oxide), or injected botulinum toxin.[10] A significant percentage (50–92%) of patients treated with a second agent after nitroglycerin failure healed without surgery. However, these are small studies.

Topical L-arginine, an intrinsic precursor of nitric oxide, has been shown to lower anal resting pressure in healthy volunteers[18] and also to heal 50% of chronic fissures without the side effect of headache.[17] However, topical nitroglycerin produces better healing rates and continues to be widely used. Orally administered

L-arginine failed to affect anal canal resting pressure or anodermal blood flow.[19]

AGENTS AFFECTING CELLULAR CALCIUM FLUX

Contraction of the internal anal sphincter is dependent on an increase in cellular ionized calcium. This is produced by direct influx of calcium through membrane Ca^{2+} channels, or stimulation of α_1-adrenoreceptors, which results in release of calcium from the sarcoplasmic reticulum. Relaxation is induced by antagonizing membrane Ca^{2+} channels or α_1-adrenoreceptors. Decrease in cytosolic Ca^{2+} produces smooth muscle relaxation. Herein lies the rationale of employing calcium channel blockers and α_1-adrenoreceptor antagonists in anal fissure treatment.

Topical calcium channel blockers (2% diltiazem, 0.3% nifedipine) have been reported to heal 65 to 95% of fissures.[20–23] The most common side effects are headache, flushing, and symptomatic hypotension. These agents can also be used in combination with other nonsurgical therapies with improved results.[9] However, there is again no commercially manufactured preparation available in the United States.

Orally administered calcium channel blockers have proved to be less promising in fissure therapy, with a lower healing rate and higher rate of side effects.[22] These are not currently being clinically used to treat anal fissures.

α_1-Adrenoreceptor blockade has been evaluated for effect on anal sphincter pressure. A single oral dose of indoramin (an α_1-adrenoreceptor antagonist) was given to seven patients with fissure and six healthy controls. This produced a drop in anal canal resting pressure of 36% in fissure patients and 40% in controls, which persisted for 3 hours.[24] However, indoramin failed to heal fissures in a subsequently performed small double-blind randomized trial.[25]

BOTULINUM TOXIN

Injection of botulinum toxin into the internal sphincter produces a temporary "chemical sphincterotomy," allowing healing of 60 to 80% of fissures after a single injection. Anal canal resting pressures are decreased for 2 to 3 months. At higher doses, squeeze pressure may also be temporarily decreased. Healing takes longer than after surgical sphincterotomy, but return to full activity occurs sooner and risk of new incontinence is essentially zero. Recurrences are common but may be retreated with a good healing rate.[26,27] There is no consensus on dose, site(s), or number of injections. Higher doses produce better healing rates and seem as safe as lower doses.[26] Topical nitrates seem to potentiate the effect of botulinum toxin in patients with refractory fissure.[28] Up to 20% of patients fail botulinum toxin therapy, and failure rates are lower if higher doses are used.[29] However, few of these studies are randomized controlled trials, and most reports contain small numbers.

COMBINATIONS OF AGENTS

Several authors have reported encouraging data using combinations of agents from the three main groups discussed previously. These are small studies, and more information is needed before a definitive answer emerges with respect to combination therapy.

OTHER AGENTS

1. Bethanechol, a *cholinomimetic that promotes synthesis of NO*, has been shown to lower anal resting pressure in volunteers. In a small nonrandomized study, bethanechol reduced fissure pain and healed 9 of 15 fissures, equivalent to topical diltiazem.[30] No side effects were noted. No long-term follow-up data are available.
2. Sildenafil (Viagra), a *phosphodiesterase inhibitor*, lowered anal resting pressure by 18% after a single intra-anal instillation of 0.75 mL of 10% sildenafil in patients with previously untreated fissures. One of 19 patients failed to respond.[31] No therapeutic data are yet available.
3. Minoxidil is a *potassium-channel opener* that induces smooth muscle relaxation and vasodilatation. A small prospective randomized study using minoxidil in treatment of anal fissure showed a healing rate of 30% or less.[32] No further therapeutic data are available.
4. In a small study, six of eight fissures refractory to other treatment healed after 15 *hyperbaric oxygen* treatments given over 3 weeks. There was one relapse at 3-month follow-up.[33] Although intriguing, hyperbaric oxygen therapy has the obvious drawbacks of cost and access and is unlikely to become a widely used modality for fissure.

Surgical Therapy

LATERAL INTERNAL SPHINCTEROTOMY

LIS is considered the treatment of choice for the surgical management of anal fissure, with healing rates of 75 to 95% reported in most series. LIS produces faster healing, less pain, and less postoperative incontinence than fissurectomy and posterior midline sphincterotomy.[34]The most concerning complication of LIS is fecal incontinence. This may be more common than previously thought: 5 to 10% for major incontinence[5–7] and up to 30% for incontinence to flatus.[8] Some authors found differences related to the patient's age, gender, and parity, but others did not. Incontinence after LIS does not appear to recover after long-term follow-up.[7] Not surprisingly, patients with postoperative continence

disturbances showed less quality-of-life improvement than those without continence alteration.[35]

Patients with anal fissures appear to be a heterogeneous population. Varying anal canal pressure profiles have been described, ranging from the classic hypertonic to normotonic and hypotonic.[36] Prior to selecting operative therapy, it is essential to obtain a complete history, including specific information on details of continence, such as soiling of undergarments, incontinence to flatus, and accidental bowel movements.[37] Recognizing the concern regarding postoperative continence alteration, several groups have reported their experience with more limited sphincterotomy—termed "calibrated," "tailored," "conservative," or "controlled." The extent of sphincterotomy is variously gauged as percentage of sphincter divided,[38] as distance below or above the dentate line,[39,40] or as unilateral or bilateral.[39] Predictably, division of more sphincter correlates with a higher incidence of impaired continence; division of less sphincter produces a higher fissure recurrence rate. Numbers in these studies are small, and follow-up is limited.

Recurrence after sphincterotomy is a particularly vexing problem for patient and surgeon. LIS can be repeated on the side opposite the first LIS, but outcome data are limited. An advancement flap procedure may be considered in this difficult situation.

ANAL ADVANCEMENT FLAP PROCEDURES

Anal advancement flap surgery has been considered an acceptable alternative to LIS,[41] but there is a lack of prospective randomized studies. A flap of well-vascularized, normally pliable skin is advanced into the strictured anal canal after excision of the fissure and surrounding fibrotic scar. This technique, which is also used for the treatment of anal stricture, is particularly attractive in patients without sphincter hypertonia; however, further study with long-term follow-up is needed.

ANAL DILATATION

Anal dilatation, manual or pneumatic, is associated with a higher fissure recurrence rate than LIS as well as a higher rate of incontinence.[34] The use of anal dilatation with medical therapy does not improve healing. Anal dilatation techniques produce uncontrolled sphincter injury[42,43] and should no longer be used.

Special Situations

Patients with Crohn's disease often have fissures that are multiple, eccentric in location, and asymptomatic. Therapy directed at the underlying cause (e.g., Crohn's disease) is often successful. A small retrospective study suggested that solitary fissures in the posterior midline may be considered for standard fissure treatment and that in selected patients healing was better after LIS than after medical fissure treatment or proximal gastrointestinal diversion.[44] Any associated suppuration should be managed appropriately.

Patients with human immunodeficiency virus or acquired immunodeficiency syndrome can develop garden-variety anal fissures, which may be treated as usual. Anal ulcers are a different clinical problem. These are usually deep with a broad base, often above the dentate line. Sexually transmitted diseases requiring treatment must be excluded. Often, appropriate antiretroviral therapy combined with attention to diet and bulking agents precludes the need for further intervention.

SUMMARY

There is a variety of acceptable treatments for anal fissure. It is important to present these to each patient in an unbiased manner and also to aid each patient so afflicted to make the best individual therapeutic choice. If a patient deems it acceptable to be symptom free, even if the fissure persists, the treatment goal chosen by the patient should guide the therapy. Although a surgeon may consider it inconvenient to apply a topical therapy thrice daily, it is the patient's opinion that matters. Avoidance of unnecessary risk remains an important goal, especially with a process that, however vexing, is completely benign.

As with many afflictions, it seems sensible and safe to begin with conservative, low-risk therapies, which can be reasonably expected to produce relief and healing in a majority of patients. These low-risk treatment options can be combined or repeated for improved outcome. More invasive treatment, which carries a higher risk, should be reserved for patients with severe disabling pain or those who are unresponsive to more conservative therapies. Evaluation of the literature reminds us that the search for the best treatment for anal fissure is ongoing as more is learned regarding possible new therapies and potential drawbacks of accepted therapies.

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