Hemorrhoids and Fissure in Ano

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• Hemorrhoids • Fissure-in-ano • Anorectal pain
• Rectal bleeding • Constipation

Hemorrhoids and anal fissures are common benign anorectal conditions that form a significant part of a colorectal surgeon's workload. In this review we summarize and evaluate the current techniques available in their management.

HEMORRHOIDS

Hemorrhoids are enlarged vascular cushions within the anal canal. They are usually found in three classical locations: left lateral, right anterior, and right posterior (3, 7, and 11 o'clock). They lie beneath the epithelial lining of the anal canal and consist of direct arteriovenous communications and surrounding connective tissue. These vascular cushions are a normal part of human anorectal anatomy, participating in the venous drainage of the anal canal. They also appear to have a role in the maintenance of continence, contributing to resting anal pressure.

Epidemiology

The exact incidence of this common condition is difficult to estimate because many patients are reluctant to seek medical advice for various personal, cultural, and socioeconomic reasons. Epidemiologic studies report a prevalence ranging from 4.4% in adults in the United States to over 30% in general practice in London. A peak in prevalence is seen between 45 and 65 years of age and the development of hemorrhoids before the age of 20 is unusual.[1–3]

Etiology

The main theories regarding the pathophysiology of hemorrhoidal disease are centered on abnormal dilatation of veins of the internal hemorrhoidal venous plexus,

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abnormal distention of the arteriovenous anastomosis, and prolapse of the cushions and the surrounding connective tissue. Increased anal sphincter pressure is also described as an etiological factor and is a reasonably consistent finding, but it is unclear if this is cause or effect.[4]

The role of mucosal prolapse in hemorrhoidal disease is uncertain. Some regard this as a completely different process, while others consider it an integral part of the hemorrhoidal disease.[5] Straining, inadequate fiber intake, prolonged lavatory sitting, constipation, diarrhea, and such conditions as pregnancy, ascites, and pelvic space-occupying lesions may contribute to development of the disease. The common factor appears to be the association with elevated intra-abdominal pressure. A family history of hemorrhoidal disease has also been suggested to be relevant, but there is no direct evidence of a hereditary predisposition and these observations are probably more related to environment.[6–8]

Classification

The dentate line gives rise to the simplest classification of hemorrhoidal disease. External hemorrhoids originate distal to the dentate line and are lined with modified squamous epithelium. Internal hemorrhoids originate proximal to the dentate line and are covered with mucosa. In some patients the two types coexist.

In Golligher's classification, internal hemorrhoids are subdivided into a further four grades according to the amount of prolapse. In first-degree hemorrhoids there is bleeding but no prolapse. Second-degree hemorrhoids may prolapse beyond the external sphincter and be visible during evacuation but spontaneously reduce. Third-degree hemorrhoids protrude outside the anal canal and require manual reduction, while fourth-degree hemorrhoids are irreducible and are constantly prolapsed. The problem with this classification is that it gives no indication of the extent of the patient's symptoms and emphasis is on prolapse.

Clinical Evaluation

Symptoms

Most patients present with painless bleeding, but some experience swelling, discomfort, discharge, soiling, or pruritus. Pain on defecation with associated bleeding is more suggestive of a thrombosed external hemorrhoid or an anal fissure. Internal hemorrhoids usually become symptomatic only when they prolapse, become ulcerated, bleed, or thrombose. External hemorrhoids may be asymptomatic or be associated with discomfort or bleeding from ulceration, or acute pain if complicated by thrombosis. Bleeding from hemorrhoids rarely causes anemia, and patients who present with anemia require further investigation of the gastrointestinal tract.[9]

Diagnosis

The diagnosis is usually simple on inspection of the perineum, rectal examination, and proctoscopy. This differentiates hemorrhoids from other anorectal pathology, such as skin tags, anal warts, fissures, fistulas, tumors, polyps, and prolapse. Large external hemorrhoids are easily seen on inspection and proctoscopy allows internal hemorrhoids to be visualized in the classical positions.

Patients over the age of 40 who have suspected hemorrhoidal bleeding cannot be assumed to have no other colorectal pathology and should be referred for a specialist opinion. Most will then require additional evaluation by flexible sigmoidoscopy, colonoscopy, CT colonography, or barium enema. Indications for formal colorectal investigation are as follows:

Iron-deficiency anemia
Positive fecal occult blood test

Age 50 years or older, with no complete colon evaluation within 10 years
Age 40 years or older, with positive family history for a single first-degree relative with adenoma or colorectal cancer diagnosed at age over 60 years and no complete examination within 10 years
Age 40 years or older, with positive family history for two or more first-degree relatives with adenoma or colorectal cancer diagnosed at age over 60 years and no complete examination within 3 to 5 years
Any history or physical finding indicating malignancy or inflammatory bowel disease

Many colorectal units in the United Kingdom now use protocols that allow direct access to investigation based on standardized proformas completed by general practitioners.

Patients with hemorrhoids and associated soiling or incontinence may require anorectal physiology studies and endoanal ultrasound as these patients have a higher risk of developing incontinence after surgery. These investigations are often instructive in tailoring treatment and in cases where surgery is being considered.

Treatment

Conservative treatment

Dietary fiber supplementation improves symptoms and is generally recommended to all patients.[10] The evidence for other lifestyle modifications, such as improving anal hygiene, taking sitz baths, increasing fluid intake, relieving constipation, and avoiding straining, is scarce, but these measures are routinely employed in the treatment and prevention of hemorrhoids.

Well-designed studies have found no evidence to support the use of any of the myriad of over-the-counter topical preparations that contain low-dose local anesthetics, corticosteroids, keratolytics, protectants, or antiseptics. The use of these agents is widespread for symptomatic relief but the long-term use of these products, particularly steroid preparations, may be detrimental and should be discouraged.

Venotonics, such as flavonoids, have been used as dietary supplements in the treatment of hemorrhoids. The mechanism of action of these drugs remains unclear. They are claimed to improve venous tone, reduce hyperpermeability, and to have anti-inflammatory effects. Meta-analysis of currently available studies does not support the use of these agents, despite their popularity in some parts of the world.[11] The Food and Drug Administration does not currently approve the use of flavonoids in the United States.[12]

Outpatient treatments

A range of interventions are available in the outpatient management of hemorrhoidal disease. These include sclerotherapy, rubber-band ligation, infrared coagulation, hemorrhoidal artery ligation, bipolar diathermy, and cryotherapy.

Sclerotherapy Injection sclerotherapy was first described 2 centuries ago and has been performed with a variety of agents but most commonly with 5% phenol. A proctoscope passed through the anal canal into the rectum is then withdrawn until the hemorrhoidal tissue prolapses into view. The submucosa at the base of the hemorrhoid is then injected with 5 mL of 5% phenol oil. The sclerosant produces an inflammatory reaction with intravascular thrombosis and submucosal fibrosis, which minimizes the extent of the mucosal prolapse and reduces the hemorrhoidal tissue.

Patients undergoing multiple injections can experience pain and discomfort. Injudicious injection of sclerosant must be avoided because it can cause chest and upper abdominal pain if injected directly into the hemorrhoidal vein[13] or cause erectile dysfunction if parasympathetic nerves are damaged.[14] Rare cases of hepatic

complications after sclerotherapy for hemorrhoidal disease have been described[15] and local infection and abscess formation are uncommon, but may occur. Antibiotic prophylaxis is indicated for patients with valvular disease or immunodeficiency as transient bacteremia is not unusual after sclerotherapy.[16]

Sclerotherapy is recommended for patients with symptomatic nonprolapsing grades I to II hemorrhoids. It is not suitable for external hemorrhoids. Its popularity has diminished, perhaps as a consequence of evidence indicating that rubber-band ligation produces superior results[17,18] and that conservative treatment with fiber supplementation may be as effective.[19]

Rubber-band ligation The technique of applying rubber bands to hemorrhoids was first described over 40 years ago. Ligation of the hemorrhoidal tissue with a rubber band causes ischemic necrosis and ulceration, which results in reduction of the prolapsed hemorrhoidal tissue and in fixation of the connective tissue to the rectal wall. Band ligation at three sites can be performed at a single clinic visit and improved banding devices allow the procedure to be performed without assistance.

The rubber bands are deployed at the base of the internal hemorrhoid proximal to the dentate line, as banding at or below the dentate can cause severe pain. Common complications include discomfort for several days after the procedure, which can be minimized by sitz baths, mild analgesics, and stool softeners. Injection of a local anesthetic does not reduce the discomfort associated with multiple banding.[20] Other complications include late hemorrhage (1 to 2 weeks after the procedure), slippage of the band, urinary retention, and, rarely, pelvic or perineal sepsis.[21–23] Rubber-band ligation is contraindicated in patients taking anticoagulants because of the risk of delayed hemorrhage.

Meta-analysis of available studies suggests band ligation is the most effective outpatient procedure for hemorrhoids,[21] providing a cure in 79% of patients with grade I to grade III hemorrhoids. Almost 20% of patients have a relapse requiring repeat banding and roughly 2% fail to respond.[24] Dietary fiber supplementation increases the long-term cure rate after banding.[25]

Endoscopic band ligation There is now increasing enthusiasm for endoscopic banding using a flexible scope,[26] as opposed to the conventional method, which employs a rigid proctoscope. Banding is performed in a manner similar to that for banding of esophageal varices. The retroflexed endoscope allows unparalleled views and photographic documentation. Multiple bands can be applied in one session, and further bands can be applied at subsequent sessions. Endoscopic hemorrhoidal ligation appears to be simple, safe, and effective. Results are good for hemorrhoids and mucosal prolapse, and the long-term recurrence rate is low (3.3%–9%).[27] The technique is at least as effective as conventional banding and may require fewer treatment sessions.[28] It has some clear advantages, apart from cost. Indications for use are the same as for conventional banding.

Infrared coagulation This technique employs infrared light, which penetrates the tissue and converts to heat with resultant coagulation and fixation of hemorrhoidal tissue. The infrared probe is applied to the apex of each internal hemorrhoid and repeated three times on each hemorrhoid. Its main limitation is that it can only be used to treat grade I and small grade II hemorrhoids.[18] If an external component is to be treated with infrared coagulation, anesthesia is needed. The main advantages are that it is painless and complications are rare. In a meta-analysis of randomized controlled trials, infrared coagulation was found to be significantly less painful than rubber-band ligation, but required more sessions to relieve symptoms, had a higher recurrence rate, and was more expensive.[21]

Doppler-guided hemorrhoidal artery ligation Doppler-guided hemorrhoidal artery ligation (DGHAL) was first described by Morinaga and colleagues[29] in 1995. This technique uses a Doppler transducer to identify hemorrhoidal arteries, allowing their selective ligation with sutures placed above the dentate line. The insertion of a ring of sutures results in a reduction of hemorrhoidal prolapse while interrupting the feeding vessels. DGHAL, which can be performed as an outpatient procedure with local anesthesia and sedation or as a day case, is successful in the treatment of grade III hemorrhoids. It appears to have none of the drawbacks of formal hemorrhoidectomy, such as pain, incontinence, or stenosis.[29–33] DGHAL does not appear to have a role in the management of grade VI hemorrhoids, but early results are promising[34] and the technique is gaining popularity. Further studies should determine its place in the management hemorrhoidal disease.

Other techniques

Electrocoagulation Bipolar diathermy and direct-current electrotherapy cause coagulation and fibrosis after local application of heat. The success rates of these methods in treating grade I and II hemorrhoids are similar to those of infrared coagulation, with relatively low complication rates.[35]

Cryotherapy Cryotherapy uses cold coagulation (nitrous oxide or liquid nitrogen) to destroy hemorrhoid tissue.[36] The procedure results in profuse, foul-smelling discharge and pain due to necrosis. Recovery is prolonged and cryotherapy is no longer recommended for the treatment of hemorrhoids.

Surgery

Surgery, in the form of formal hemorrhoidectomy, is associated with pain and the risk of uncommon but serious complications of incontinence and anal stenosis. Indicated in less than 10% of patients referred for specialist treatment, it is generally reserved for (1) grade III hemorrhoids not responding to banding, (2) grade IV hemorrhoids (prolapse), (3) large external hemorrhoids or combined internal and external components, and (4) concomitant anorectal pathology requiring surgery.

Surgical hemorrhoidectomy is a very effective treatment with high cure and low recurrence rates. These procedures are now performed in a day-surgery setting in many centers.

Hemorrhoidectomy Excisional hemorrhoidectomy can be performed as an open or closed procedure. In the United Kingdom, the Milligan-Morgan hemorrhoidectomy is the most commonly performed. The hemorrhoid is dissected off the anal sphincter, its vascular pedicle ligated, and the wounds left open to heal by secondary intention with skin and mucosal bridges. The Ferguson hemorrhoidectomy is favored in the United States. The hemorrhoid is exposed in the anoscope, then excised and ligated, and the wounds closed.[37]

Four randomized trials have compared open versus closed hemorrhoidectomy.[38–41] Both techniques are safe and effective, with no consistent difference in postoperative pain, analgesic use, hospital stay, or complication rates. Wound healing showed mixed results, as dehiscence of primarily closed wounds prolonged healing times beyond that of the open technique.

The Harmonic Scalpel and LigaSure have been employed in excisional hemorrhoidectomy. These instruments allow the procedure to be performed more rapidly and provide a dry operating field, but do not appear to offer any other specific advantages and randomized controlled trials show no improvement in postoperative pain.[42–45] These methods have the obvious disadvantage of increased costs.

The complications of hemorrhoidectomy include urinary retention (2%–36%); bleeding (0.03%–6%); infection (0.5%–5.5%); anal stenosis (0%–6%), usually as a result of inadequate mucosal bridges; and incontinence (2%–12%).[21] Sphincter defects associated with incontinence have been documented by endoanal ultrasound and manometry in up to 12% of patients after hemorrhoidectomy.[46–49]

Postoperative pain remains a significant problem and most patients do not return to work for 2 to 4 weeks after surgery.[46] Local anesthesia, glyceryl trinitrate (GTN) paste, and simultaneous lateral internal sphincterotomy have been attempted to reduce postoperative pain without convincing benefit.[50–54] Sphinterotomy should not be performed as it exacerbates continence impairment.[55] Postoperative analgesics, laxatives, and prophylactic metronidazole appear to reduce pain and convalescence after day surgery.[56]

Stapled hemorrhoidopexy Longo developed the stapled hemorrhoidectomy or hemorrhoidopexy in the mid-90s and since then it has gained popularity, particularly in the Far East. The procedure is also known as the procedure for prolapsed hemorrhoids and stapled anopexy. The technique employs a circular stapler, which performs a circumferential resection of mucosa and submucosa above the hemorrhoids, stapling the defect closed with a single firing of the staple gun. The prolapsing hemorrhoidal tissue is resuspended back into the anal canal and the arterial inflow is interrupted in a manner similar to that for DGHAL. The hemorrhoids are not removed, but rather returned to their normal anatomic position.

There are no wounds, less incontinence, less pain, and a shorter recovery period compared with excisional hemorrhoidectomy.[57] Recurrence rates are higher and, although complication rates are no higher than those for conventional hemorrhoidectomy, a number of serious complications were documented following the introduction of the stapled hemorrhoidopexy.[58] These included bleeding, rectal perforation, rectovaginal fistulas, occlusion of the rectum, and perineal and severe pelvic sepsis.[59] Similar complications have been described for most treatments for hemorrhoidal disease. A recent Cochrane systematic review[60] concluded that the procedure was as safe as conventional hemorrhoidectomy but that its main drawback was recurrence. Consequently, with the procedure for prolapsed hemorrhoids, the need for further subsequent procedures is comparable to that for excisional hemorrhoidectomy.

The main role for the procedure for prolapsed hemorrhoids appears to be in the treatment of grade II and III hemorrhoids that have failed outpatient treatment. It may have a role in treating grade IV hemorrhoids that are reducible under anesthesia, but recurrence in this situation appears to be a problem.

Acutely thrombosed hemorrhoids The management of hemorrhoids in an elective setting has been emphasized in this review but patients occasionally present with acutely thrombosed prolapsed hemorrhoids as an emergency. This is a very painful condition that most surgeons would manage, at least initially, with a conservative approach. Ice packs, stool softeners, local anesthetic cream, metronidazole, and ditiazem can be helpful. Emergency surgery is occasionally required for those patients who do not settle, but can be associated with significant morbidity.[61,62]

The management of hemorrhoids in certain special situations in summarized in **Fig. 1**.

Summary

Hemorrhoids remain a common problem and comprise a significant percentage of a colorectal surgeon's workload. A wide and still expanding range of procedures to

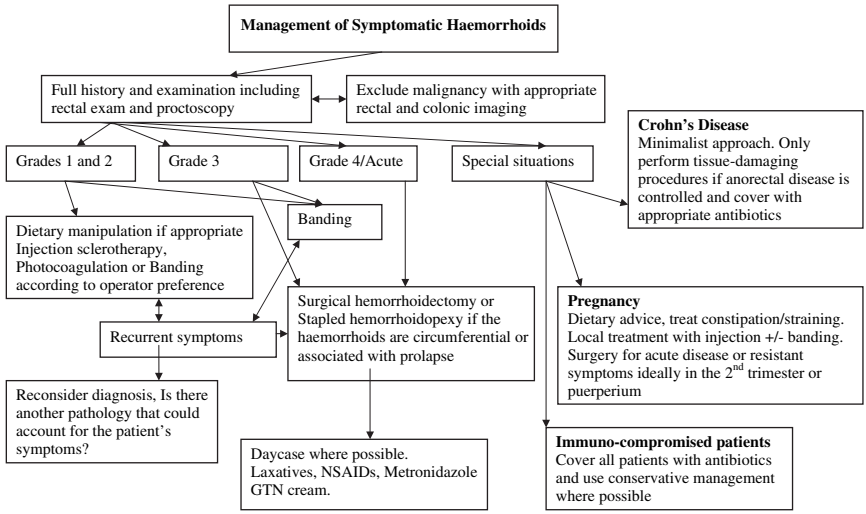

Fig.1. Management of anal fissure. (*From* Steele SR, Madoff RD. Systematic review: the treatment of anal fissure. Alimentary Pharmacology & Therapeutics 2006;24(2):247–57; with permission.)

treat the condition have been developed and the data generated from studies comparing one technique to another is overwhelming (**Table 1**).

It is safe to say that no one treatment is a panacea. Hemorrhoidal disease is a heterogeneous condition that requires the surgeon to select the most appropriate treatment for the problem that the patient presents. The treatment of hemorrhoidal disease should therefore be tailored to the individual.

FISSURE IN ANO

An anal fissure is a painful tear or split in the distal anal canal. Patients typically complain of severe anal pain during and after defecation, lasting minutes to hours. Bleeding, in the form of bright red blood, is commonly seen either on the toilet tissue or streaking the stool surface.

Table 1
Treatment options for hemorrhoidal disease

Treatment	Indications	Evidence Grading
Sclerotherapy	Grades I and II	Level 1
Rubber-band ligation	Grades I, II, and III	Level 1
Endoscopic banding	Grades I, II, and III	Level 2
DGHAL	Grades II and III	Level 2
Electrocoagulation	Grades I and II	Level 2
Cryotherapy	No current role	
Hemorrhoidectomy	Grades II–IV, external	Level 1
Stapled hemorrhoidopexy	Grades II–III	Level 1

Anal fissures may be classified as acute or chronic according to length of symptoms and typical morphologic appearances. The majority of acute fissures heal spontaneously, but a proportion become chronic and this is usually defined as a persistence of symptoms beyond 6 weeks or by the presence of visible transverse internal anal sphincter (IAS) fibers at the base of a fissure. Associated features include indurated edges, a sentinel pile, and a hypertrophied anal papilla. The medical community should establish clear classifications for fissures. It is likely that the absence of accepted definitions for chronic fissures has led to widely differing healing rates with various interventions reported in the literature. Lindsey and colleagues[63] have described a chronic anal fissure as ''the presence of visible transverse internal anal sphincter fibers at the base of an anal fissure of duration not less than 6 weeks.''

Anal fissures are most commonly seen in the posterior midline, although 10% to 20% in women and 1% to 10% in men are located in the anterior midline. Fissures located off the midline suggest the presence of underlying pathology, such as Crohn disease, syphilis, or anal cancer, and generally require further evaluation with an examination under anesthesia and biopsy to establish a diagnosis.[64]

Chronic fissures are associated with IAS spasm and ischemia, the relief of which is central to achieving healing whether a surgical or medical approach is taken.[65]

Pathogenesis

The exact mechanism surrounding the pathophysiology of anal fissures has not been clearly established. The current hypotheses are centered on anal sphincter tonicity and blood flow.

It is thought that the initiating factor is trauma to the anal canal, possibly due to the passage of hard stool, but constipation is not always reported and some patients describe repeated episodes of diarrhea. Constipation, by repeated aggravation of the anal canal, is likely to play a role in perpetuating an anal fissure. Increased resting pressures within the IAS in patients with fissures[66–70] has been described as another perpetuating factor and anorectal manometry has consistently demonstrated that IAS tone as measured by the resting pressure is elevated in fissure patients versus controls.[71,72] Maximal voluntary contraction of the external anal sphincter remains similar between the two groups and the IAS alone seems to be responsible for the hypertonicity.[73] There is relative ischemia in posterior midline of the anal canal[74] and this is exacerbated by increased tone, a key factor in preventing fissures from healing.

Internal Anal Sphincter Physiology

The understanding of the physiology of the IAS has improved significantly in recent years and this provides the rationale for current nonsurgical treatment.

The resting tone of the IAS depends on intracellular calcium concentration, and contraction of the smooth muscle cells within the IAS is mediated by influx of calcium through calcium channels and by stimulation of α1-adrenoreceptors at the smooth muscle cells.

Activation of α2-adrenoreceptors in the myenteric inhibitory neurons presynaptically inhibit nonadrenergic, noncholinergic (NANC) relaxation. Relaxation of these cells is mediated through directly decreasing intracellular calcium concentration as well as increasing cyclic guanosine monophosphate and cyclic adenosine monophosphate. Potassium influx hyperpolarizes the cell membrane and decreases calcium entry. In addition, inhibitory neurotransmitters, such as nitric oxide and vasoactive intestinal peptide, mediate NANC relaxation. Nitric oxide is the major neurotransmitter mediating NANC relaxation of the IAS.[75,76] L-arginine, a precursor of nitric oxide, has been found to relax IAS smooth muscle perhaps by increasing substrate for nitric oxide

synthase, the enzyme involved in nitric oxide synthesis.[77] A preliminary study has shown reduced nitric oxide synthase in the IAS of patients with anal fissures compared with controls.[78] The reduced production of nitric oxide provides a possible explanation for the high IAS pressures seen in most fissure patients and also why pressures return to pretreatment values in patients whose fissures have healed with medical treatment. The ''chemical'' sphincteromy lasts only as long as the treatment is continued.[79]

Treatment

Conservative management

The aim of treatment of an acute fissure is to break the cycle of a hard stool, pain, and spasm. This can be accomplished by adequate fluid, fiber, and, if necessary, stool softeners. Up to 90% of patients diagnosed with acute fissures heal with these measures alone, but chronic fissures usually require medical or surgical therapy.

Medical therapy

Increased understanding of anal sphincter physiology, coupled with concerns regarding long-term impaired continence as a consequence of surgery, has driven enthusiasm for pharmacologic treatments for chronic anal fissure. These agents have been developed with the aim of creating a reversible reduction in the abnormally high resting sphincter pressure until the fissure has healed.

Glyceryl trinitrate GTN was the first pharmacologic treatment used in creating a ''chemical sphinterotomy.'' Nitrates are metabolized by smooth muscle cells to release nitric oxide, the principle nonadrenergic, noncholinergic neurotransmitter in the IAS. Its release results in IAS relaxation and increased anodermal blood flow. The usual course is 0.2% GTN, applied topically two or three times daily, for 8 weeks.

The first randomized trial involved patients receiving 0.2% GTN (twice daily for 8 weeks) or placebo.[80] Healing rates were significantly higher in the GTN than in the placebo group (68% versus 8%; $P < 0{\cdot}001$). Perhaps unsurprisingly, there followed great enthusiasm for topical GTN. The treatment significantly reduces pain on defecation after 2 weeks, even in patients who don't heal. Repeated applications may be necessary and are safe. Higher dosing does not improve outcome but, interestingly, does not appear to worsen side effects.[81–83] The most common of these are headache (27%) and hypotension (6%).

However, subsequent trials did not replicate the initial positive results and healing rates are lower than expected with one Italian study demonstrating no difference compared with placebo.[84,85] Medium-term relapse is a problem, side effects common, and compliance is uncertain. The overall healing rate in Nelson's recent Cochrane meta-analysis is 48.6% compared with 37% with placebo, but late recurrence is common, in the range of 50% of those initially cured.[86] The high rates of failure mean that the question of how to treat GTN-resistant fissures is significant. Despite this, GTN is safe, readily available, and has a modest but significant effect compared with placebo. It remains first-line treatment in many centers.

Calcium channel blockers Calcium channel blockers prevent influx of calcium into smooth muscle cells, decreasing intracellular calcium and preventing smooth muscle contraction with a consequent reduction in resting IAS pressure.[87–90] Oral agents appear to have poorer healing rates and higher rates of side effects than topical preparations. Topical calcium channel blockers (diltiazem 2%, nifedipine 0.3%) achieve fissure healing to a degree similar to that reported for topical nitrates, but with fewer side effects and better compliance.[91] Recurrence rates after long-term follow-up appear to be no better than treatment with GTN.

Botulinum A toxin injection Derived from exotoxin produced by the bacterium *Clostridium botulinum*, botulinum A toxin is a potent neurotoxin. Its effects on smooth muscle are well documented and, when injected into the IAS,[92,93] it produces a chemical denervation of motor end plates with a subsequent decrease in resting anal pressure and improved perfusion. The treatment is more invasive than the topical ointments but does not have the same problems with compliance and can be performed in an outpatient setting. It provides a reversible chemical sphincterotomy and represents a novel nonoperative treatment in the management of chronic anal fissure. Side effects, such as temporary minor incontinence and urgency, appear to be infrequent and reversible. Its major disadvantage is its cost, but this has to be set against the cost of surgery.

In one prospective randomized trial that compared injection of 20 U of botulinum toxin with 0.2% GTN twice daily, the botulinum toxin group was associated with significantly improved healing rates (96% versus 60%, $P = .005$).[94] Similar prospective studies, while not achieving such successful rates of healing, have found approximately 80% of patients with initial healing at 6 months.[95,96]

The issue of recurrence after botulin toxin injection remains to be determined and there is still debate regarding the ideal location of injection (into the IAS, external anal sphincter, or the intersphincteric groove) and optimal dose. A number of studies use 20 U divided in one to four injections but there is evidence that higher doses can give better results. In combined analyses botulin toxin was found to be no better or worse than topical nitrates,[97] but botulin toxin is effective in healing 50% to 70% of patients with fissures resistant to topical nitrates,[98] and it may have a role in the treatment of refractory fissures either alone or in combination with topical nitrates.[99]

A Cochrane review of nonsurgical therapy for anal fissure has concluded that medical therapy for nonhealing fissures may be applied with a chance of cure that is marginally but significantly better than that for placebo, but far less effective than surgery and a high recurrence rate.[97] Nonetheless, the risk of using such therapies is not great, without apparent long-term adverse effect, and treatment can be repeated. Medical treatment can therefore be used in individuals wanting to avoid surgery, with surgery being reserved for treatment failures.

Other nonsurgical treatment

A variety of other agents have been used in the treatment of anal fissures. These include the nitrous oxide precursor L-arginine,[100] alpha-1 receptor antagonists,[101] angiotensin-converting enzyme inhibitors,[102] and hyperbaric oxygen.[103] None has demonstrated advantages over currently available therapy and data is limited at present.

Surgery

Surgery represents traditional management of chronic anal fissure. Manual dilatation and internal sphincterotomy have been employed to create a permanent reduction in resting anal pressure.

Manual dilatation of the anus Manual dilatation was once first-line treatment for chronic anal fissure. The aim was to reduce sphincter tone by controlled manual stretching of the internal sphincter. A variable number of fingers are inserted into the anal canal and lateral distraction exerted on the sphincter and sustained for a period. This procedure frequently produced an uncontrolled tearing of the sphincter muscles resulting in incontinence, with characteristic findings on anal endosonography.[104–106]

Speakman and colleagues[104] evaluated 12 men with fecal incontinence after manual dilatation and found that 11 had gross internal sphincter disruption and

3 had associated external sphincter damage. Both prospective[105–109] and retrospective[110–112] studies have documented the risk of incontinence after manual dilatation. Incontinence to flatus is of the order of 0% to 27%. Anal stretch, in its classical form, carries a higher risk of fissure persistence or recurrence and of impaired continence compared with internal sphincterotomy.[113] There is no role for its continued use in the modern management of anal fissure.

However, the concept of anal stretch has been revisited more recently using controlled balloon dilatation with a standardized protocol that overcomes the problem of reproducibility. Limited available data suggest results comparable to those for lateral internal sphincterotomy.[114] Further studies are required to evaluate this technique.

Lateral internal sphincterotomy Internal sphincterotomy was first described by Eisenhammer in 1951.[115] The original method of dividing internal anal sphincter muscle in the posterior midline fissure bed often led to a ''keyhole'' or ''gutter'' deformity with associated impaired continence. Lateral internal sphincterotomy (LIS) was then developed by Notaras.[116] The procedure remains the surgical treatment of choice for management of anal fissures refractory to nonsurgical therapy and may be offered without a trial of pharmacologic treatment.[116,117]

The procedure involves division of the internal anal sphincter laterally as an open procedure under direct vision or blindly through a stab incision.[118–120] The length of IAS divided varies, with some surgeons dividing muscle from the distal end of the fissure to the dentate line and others taking muscle equal in length to the fissure,[121] an approach that attempts to diminish the risk of impaired continence. The fissure itself does not require excision or fissurectomy as this encourages deformity. LIS may be done with the patient under local, regional, or general anesthesia, and can be combined with other procedures for concomitant anorectal pathology.[122]

LIS is effective in healing anal fissures with rates of 90% to 100% and low recurrence (1%–3%), but this comes with a price of risk of incontinence, the incidence of which has been variably reported from 0% to 50%.[123] However, incontinence sufficient to cause any measurable impairment in quality of life is uncommon, in the range of 3% to 5%,[124,125] but, unlike continence impairment on medical therapy, it may be permanent. Outcome data on these patients is surprisingly absent and no study has compared incontinence after LIS with other groups with continence impairment.

It is unclear why some series report such high incontinence rates after LIS. The procedure appears to be well controlled with careful division of muscle under vision but it seems that standardization and reproducibility are problems, just as they are with manual dilatation. Sultan and colleagues[126] evaluated the extent of sphincterotomy with the use of anal ultrasonography and showed a high incidence of inadvertent full-length division of the IAS, a problem that appears to be more common in women as a result of overestimation of the length of the shorter female IAS. Farouk and colleagues[127] investigated patients with persistent fissures after LIS by anal ultrasonography and revealed that over 70% had no internal sphincter defect, whereas several had incurred an external sphincter defect. It seems reasonable to conclude that the wide range of continence impairment after LIS may be a function of disparate surgical techniques among units and individual surgeons. Patient selection likely plays a role because others have documented on anorectal physiology and ultrasound unexpected obstetric injuries after LIS.[128]

Patients with preoperative incontinence problems should not undergo LIS and relative contraindications include those with irritable bowel syndrome or diabetes and elderly or postpartum women. Women with a prior obstetric injury and

a nonhealing fissure present a difficult problem and it is inadvisable to proceed with LIS in such patients without satisfactory preoperative anal manometry and endoanal ultrasound.

There is no rationale for LIS in patients with a fissure and normal or subnormal IAS tone as hypertonicity is not an issue in this subgroup.[129] Patients with low-pressure fissures and those with significant birth injuries are probably better served with an anal advancement flap.[130,131]

Summary

The choice of treatment remains difficult. Surgery is very effective but high healing rates come with the risk of continence impairment. Publications on treatment and outcome for incontinence after sphincterotomy for fissure are absent and so the duration and magnitude of this problem are uncertain. Medical therapy with GTN is safe and represents a good first line of treatment. The 30% to 50% of patients with chronic fissures resistant to GTN can subsequently be offered second-line treatment with topical diltiazem or botulinum toxin injection and, in some cases, lateral internal sphincterotomy. Patients at high risk of continence disturbance should be identified and evaluated by anorectal manometry and ultrasound before surgery is offered. All patients considered for surgery should be fully cognizant of the potential risks and benefits before giving informed consent as some may wish to persist with an alternative medical therapy.

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