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## Abbreviations

BT	Botulinum toxin
GTN	Glyceryl trinitrate
IAS	Internal anal sphincter
ISDN	Isosorbide dinitrate
NO	Nitric oxide

## 5.1 Etiology

Anal fissure is a painful tear in the posterior or anterior epithelial lining of the anal canal distal to the dentate line. It is a highly distressing and common condition that affects different age groups, but most commonly in young adults (20-30 y.o.).

Although there are several theories about the origin of anal fissure, none of them is accepted as the unique cause; the etiology is probably multifactorial. For many years it was believed that trauma to the epithelium of the anal canal created by the passage of hard stools was the main cause. This initial trauma would be followed by pain and an increase in the internal sphincter tone,

which in turn aggravated the pain during defecation—thus a vicious cycle was created. This theory, although simple and easy to understand, is not convincing because a history of hard stools is found in less than 25% of patients with fissures; furthermore, almost 10% of patients have diarrhea.

The two main factors associated with anal fissure are an increase in the internal sphincter tone and a decrease in blood flow in areas of anodermal epithelia. Manometric studies have demonstrated that patients with anal fissure have an increased resting anal pressure and a decrease of spontaneous relaxation of the internal anal sphincter (IAS) [1]. Similarly, some reports mention tissue ischemia as the initial mechanism of anal fissure. This theory is based on studies showing an important decrease of blood flow in the posterior part of the anal canal seen on Doppler laser flowmetry [2]. This low blood flow was also demonstrated in the anterior midline part, but not in the lateral quadrants, when compared with controls. These two theories are actually complementary and assist in the treatment of a chronic anal fissure. Decreasing the tone of the IAS significantly improves the irrigation of the ischemic area, causing the ulcer to heal gradually and symptoms to improve [3].

Recent studies also suggest a different pathophysiology for posterior and anterior anal fissures. Patients with an anterior anal fissure who

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developed anal incontinence after sphincterotomy have been found to have an occult external anal sphincter injury and impaired external anal sphincter function compared with patients with posterior fissures [4]. These groups of patients are typically younger women, and their maximum squeeze pressure has been found to be significantly lower when compared with the posterior fissure group. More studies are needed to support these findings. Furthermore, postpartum fissures cause no increased anal tone and are probably caused by constipation and birth trauma.

Most fissures (90%) arise in the posterior midline. An anal fissure occurs in the anterior midline in 10% of affected men and up to 25% of affected women. Accordingly, when there are multiple fissures or the fissure is located in the lateral position, other etiologies have to be investigated: anorectal trauma, Crohn's disease, infections (e.g., tuberculosis, HIV/AIDS, herpes, syphilis), anal or rectal cancer, and dermatologic diseases (e.g., psoriasis).

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## 5.2 Incidence

Although multiple publications note that anal fissures are common, there are not many reliable estimates of the frequency of anal fissures among the general population. An overall incidence of 1.1 per 1,000 person-years has been recently published [5]. This incidence translates to an average lifetime risk of 7.8%, which positions anal fissure as a real common health problem.

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## 5.3 Epidemiology

Sex distribution shows almost no differences, although it is slightly more common in women. While anal fissure is a common cause of anal bleeding in children, the peak incidence occurs during adolescence and young adulthood in women, and during middle age among men. Constipation, hypothyroidism, obesity, pregnancy and weight loss have been associated with anal fissure [5].

## 5.4 Classification

An anal fissure can be classified in terms of its time of evolution (acute or chronic) or by the pathophysiologic cause (primary or secondary). Classification as primary or secondary is important because treatment is different and directed toward its cause. Primary anal fissures are treated with the objectives of decreasing anal sphincter tone and increasing blood flow. Secondary anal fissures are the result of several causes, including malignancy (anorectal cancer, leukemia), inflammation (Crohn's disease), infections (HIV/AIDS, herpes, tuberculosis, syphilis), anorectal trauma, or dermatologic conditions (psoriasis). The specific cause of secondary anal fissure must be accurately treated.

The treatment of anal fissure also follows multiple stages, from dietary modifications to medical therapy to surgical procedures. Nonoperative therapy is the first option; surgical treatment is reserved for failures or complications. If an acute fissure does not heal and lasts more than 6–8 weeks, it is then considered to be chronic. The grade of pain or bleeding does not distinguish between acute or chronic fissure, but the duration of symptoms and clinical aspects do. Acute fissures are usually superficial, and the tear appears pink to red. Chronic fissures are deeper; the transverse fibers of the IAS are exposed and chronic granulated tissue is seen on its base. A sentinel pile and a hypertrophied anal papilla can be present (Fig. 5.1). Anal fissures are also classified as chronic if the secondary lesions mentioned above (e.g., deep scar, exposed internal sphincter, pile, and papilla) are present.

Coloproctologists will probably see more chronic than acute fissures because primary care physicians and emergency surgeons can treat and heal most acute anal fissures with conservative measures and nonsurgical interventions.

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## 5.5 Diagnostics

Anal fissure is usually diagnosed through the history and a physical examination. Pain is the hallmark of anal fissure symptoms. Pain starts



**Fig. 5.1** Anal fissure. Internal anal sphincter at the base of the fissure (Courtesy of Dr. J.V. Roig)

during defecation or sometimes just after a bowel movement and can last from minutes to several hours. Patients frequently describe the pain as spasms or as if they were “passing glass”; the intensity of the pain while defecating enhances the fear of doing so, predisposing patients to constipation, harder and drier stools, and worse trauma. Rectal bleeding is frequent, minimal, bright red, and not related to the severity of the anal fissure.

Inspection with gentle traction of the buttocks often shows the fissure (Fig. 5.2). If a fissure is diagnosed during the initial consultation, other maneuvers (rectal examination or endoscopy) are not indicated in most patients at that time to avoid causing or increasing the existing pain. If a fissure is not observed, then an examination under anaesthesia should be advised to make the correct diagnosis and to rule out ano-rectal sepsis. Atypical fissures (lateral, non-healing, painless, or multiple) are more appropriately managed with examination under anaesthesia, and a biopsy and culture should be evaluated.

Anoscopy, endoscopy, or rectal examination, if indicated, should be delayed if possible until symptoms resolve. Anal manometry is not recommended as a routine initial exploration because it can cause or aggravate the pain and is normal or low in 19% of evaluated men and 42% of affected women.



**Fig. 5.2** Exposition of an anal fissure

## 5.6 Medical Treatment

Initial treatment of anal fissure includes dietary modifications, local measures, and pharmacological therapy. The first line of therapy is directed toward relaxing the IAS with the use of warm sitz baths. Also, modifying stool consistency to reduce trauma while passing stool can be achieved by increasing fluid and fiber intake both to avoid hard stools and to prevent diarrhea. Medical intervention should also be directed at relaxing the increased tone of the IAS and improving blood flow in the affected area. Surgery is indicated in cases of treatment failure or complications [6, 7]. The success of these general measures without accompanying drug treatment is 87% in cases of acute anal fissure (but only 30% in recurrences) and less than 50% in cases of chronic anal fissure. The use of anaesthetic ointments does not improve the results of these conservative measures.

The main pharmacological treatments for anal fissure are nitric oxide (NO) donors, calcium

channel antagonists, and botulinum toxin (BT). The objectives of these measures are to reduce anal sphincter tone and to increase blood flow to the anal area.

### 5.6.1 Nitric Oxide Donors

Glyceryl trinitrate (GTN) and isosorbide dinitrate (ISDN) are the NO donors used to treat anal fissure. These are administered topically to the anal skin with the aims of relaxing the IAS and increasing local blood flow. GTN has been applied at two different concentrations: 0.2% and 0.4%. ISDN needs to be administered five times a day to achieve the same amount of nitrate that GTN provides with only two applications a day (although in published studies GTN is applied at a 1% concentration three times a day) [8]. This is why ISDN is not routinely used in practice. GTN at a concentration of 0.4% has been marketed in Europe. The topical application of GTN is associated with transient headache in 27–50% of patients [8]. These may occur during the first 2 or 3 weeks of treatment and last between 10 and 30 min. The headaches usually respond to standard treatment with pain killers, but 10–20% of patients abandon GTN treatment because of the headaches [6]. The pain caused by the anal fissure begins to improve between the fifth and seventh days, but the treatment must be maintained for minimum of 8 weeks to increase the chances of a cure. A meta-analysis of 75 studies showed that GTN has a better rate of healing of anal fissure than placebo (48.6% vs. 37%;  $P=0.004$ ) [8].

The figures published on recurrence are diverse and range between 17% and 67% [9–13]. A significant proportion of patients with long-term recurrence can be treated again with topical GTN or other topical medications, and surgery is not always necessary. In fact, the number of surgeries for anal fissure has decreased in recent years to between 60% and 72%.

Patients with a risk of hypotension and those taking sildenafil (Viagra) or another type of phos-

phodiesterase type 5 (tadalafil [Cialis], vardenafil [Levitra]) inhibitors should be treated with medications different from GTN because of such risk.

### 5.6.2 Calcium Channel Antagonists

Calcium channel antagonists such as nifedipine and diltiazem have been shown to relax the IAS and decrease resting pressure in the anal canal [14]. These drugs have been administered both orally and topically. Oral forms increase the risk of dizziness and episodes of significant hypotension in up to 5% of patients and are not more effective than topical forms [15, 16]. Calcium channel antagonists are generally used as the first-line treatment or in patients resistant to treatment with GTN.

There is no commercial preparation available in Europe, so calcium channel antagonists must be compounded (custom-made) and prescribed as formulations: either diltiazem 2% or nifedipine 0.2–0.5%. Prescriptions are generally associated with lidocaine (a local anaesthetic) to help with the pain caused by the anal fissure. Their effectiveness is difficult to assess based on the literature because of the small number of publications and their short follow-up, but studies comparing nifedipine and diltiazem with GTN show that calcium channel antagonists are at least as effective as GTN (50–65%), with a similar incidence of recurrence and fewer adverse effects (flushing, headache) [18, 19]. Headache occur in only 0–25% of patients, that is, half of the prevalence when compared with GTN (33–50%) [17].

A systematic review of studies comparing diltiazem and GTN included 481 patients. It concluded that their effectiveness and relapse rates are comparable, but the diltiazem group showed fewer adverse effects (Risk ratio (RR)=0.48; 95% CI=0.27–0.86;  $P<0.01$ ) [20].

ISDN has also been compared to surgery; in a large study involving 207 patients with chronic anal fissures, success at 6 months was 77% (ISDN) and 97% (surgery). Recurrence at 12 months occurred in 4.8% (ISDN) and 1% (surgery). De novo fecal incontinence was diag-

nosed in 6 patients (3%) of those treated with surgery and in none of the patients treated with ISDN [21].

### 5.6.3 Botulinum Toxin

BT is a protein synthesized by the bacterium *Clostridium botulinum* that has neuro-paralyzing effects. BT treatments are used to induce muscle paralysis through temporal local denervation of the treated muscles secondary to inhibition of the release of acetylcholine at the neuromuscular junction. There are various types of BT (A, B, C, D, E, F, and G); type A BT is currently used in the treatment of anal fissure.

There are several commercial presentations of BT. Those used in the treatment of anal fissure are botulinum toxin type A (Botox; 50 or 100 IU/vial), incobotulinumtoxinA (Xeomin; 50 and 100 IU/vial), and abobotulinumtoxinA (Dysport; 500 IU/vial). When Dysport is used it should be remembered that dosing is on a ratio of approximately 1 to 3, meaning that 50 IU of Botox or Xeomin have the same effect as 150 IU of Dysport [22]. Correct administration of BT is followed by local muscle relaxation that lasts around 2 to 4 months.

BT has been injected in different ways—unilateral or multilateral, at the base of the fissure or at one or both sides of the fissure, at the IAS, in the external anal sphincter, or both—and at different doses: from 5 to 50 IU (most commonly 50 IU) in single or multiple applications. This large variation in administration makes interpreting the results described so far difficult.

The first published results on the effectiveness of BT described a success rate over 80% [22], but subsequent studies have shown that healing is accomplished in around 50% of patients when follow-up is longer than 12 months [3, 23].

Local complications occur in less than 5% of patients and include local hematoma or infection at the site of administration. General complications are toxin allergy or temporary incontinence (0–13%), all of which are not frequent but dose dependent.

A meta-analysis including more than 270 patients demonstrated the superiority of surgery

when compared with BT (RR = 1.31; 95% CI = 1.50–1.57), a greater absolute benefit from surgery (23%), and a higher recurrence with the toxin (RR = 5.83; 95% CI = 2.96–11.49). Surgery was associated with increased rates of fecal incontinence (RR = 0.08; 95% CI = 0.01–0.59) [24]. The benefits of BT treatment are ease of application, even in a doctor's office. The main disadvantage is the high cost.

Comparative results of BT against a combined treatment of GTN and BT in patients who did not respond to ISDN did not show the superiority of the combination. Although the association had a better cure rate after 6 weeks of treatment (66% vs. 20%), this superiority was not found at the 8th (73% vs. 73%) or at the 12th week of treatment (60% vs. 66%) [25].

NO donors have also been compared with BT in several studies. A recent study with a small number of patients compared BT (Dysport 60 IU) with ISDN. Toxin cure rates were higher and adverse effects were fewer than those observed with ISDN, although recurrence rates were high in both groups (50% and 28%, respectively) [26]. GTN and BT have also been compared in several studies. A meta-analysis of these studies concluded that the two treatments are equally effective, but incontinence after treatment is more common in patients treated with BT. BT is a more invasive treatment and also has a higher cost—these are reasons why many groups consider BT as a second-line treatment, for use in cases where topical treatment has not been effective [8].

Diltiazem was compared with BT in a randomized study with 143 patients. The two treatments were equally effective in the treatment of chronic anal fissure: a healing rate of 43% was found for both treatments and a significant reduction in pain occurred in 78% (diltiazem) and 82% (BT) [27].

## 5.7 Surgical Treatment

Surgery is the definitive treatment of anal fissure. It is offered as a first treatment in patients without a risk of incontinence, although nowadays most

physicians propose it only to patients who do not respond to medical treatment or those who develop complications with medical therapy. Several surgical treatments have been described, but there is no doubt that the gold standard is still the lateral internal sphincterotomy, a section of the distal part of the internal sphincter.

### 5.7.1 Sphincterotomy

There are two different techniques described for a sphincterotomy: posterior and lateral, depending on the sectioned part of the internal sphincter. Posterior sphincterotomy, although used in the past, is not recommended today because it produces a keyhole deformity in the anus that is related to postoperative soiling. It is only performed in patients with a posterior anal fissure associated with intersphincteric abscess.

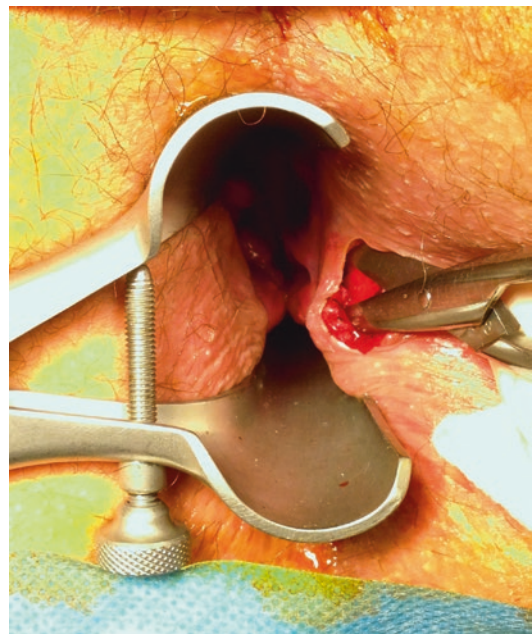
Lateral sphincterotomy is more effective than medical management; a greater than 90% chance of cure and the patient satisfaction rate support this conclusion. It can be done under local anesthesia and is mostly performed as a same-day surgical procedure.

Sphincterotomy can be performed using an open or a closed technique. When both techniques were compared, no significant differences were found, although the open technique is related to superior healing rates but increased flatus incontinence [6].

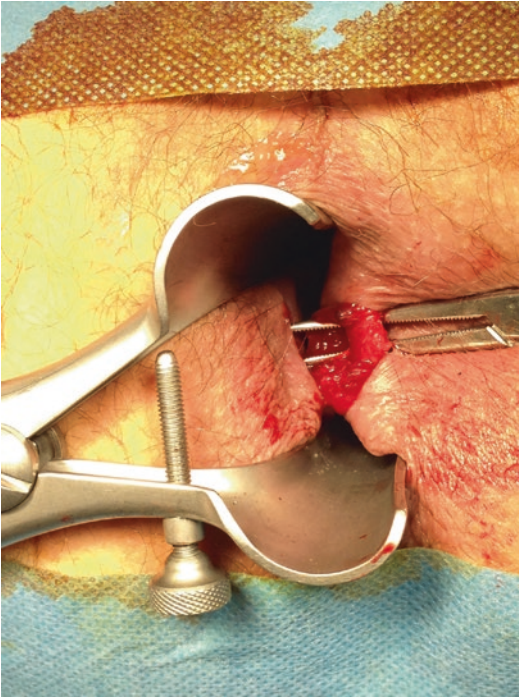
Lateral sphincterotomy is more easily performed with the help of an anal retractor to correctly identify the intersphincteric groove. An incision is made at this level in the lateral quadrant of the anus (3 o'clock for right-handed or 9 o'clock for left-handed surgeons). The incision can be either circumferential or radial; there are no differences among the short- and long-term results when both have been compared [28]. Dissection of the internal sphincter from the anal mucosa and the external sphincter is followed by a partial section of the internal sphincter. No differences in healing or complications have been found when comparing suturing versus no suturing of the skin (Figs. 5.3, 5.4, 5.5, 5.6, and 5.7).



**Fig. 5.3** Anal retractor to expose the intersphincteric groove



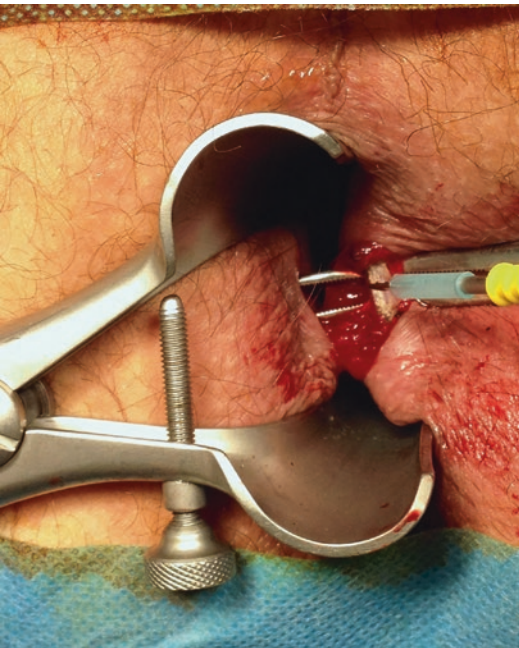
**Fig. 5.4** Dissection of the internal sphincter from the anal mucosa



**Fig. 5.5** Dissection of the internal anal sphincter



**Fig. 5.7** Final aspect of the wound after lateral sphincterotomy



**Fig. 5.6** Section of the internal anal sphincter

With respect to the internal sphincter section, limiting it to less than half the length of the sphincter does not increase the recurrence rate and diminishes postoperative fecal incontinence, although some groups recommend a more economical length of division at less than 25 % of its length, which in women corresponds to less than 1 cm [29].

When performing a lateral sphincterotomy, a tear produced while dissecting the anal sphincter from the anal mucosa is best solved by opening the entire involved mucosa, as in a lay-open technique, to avoid creating a postoperative fistula.

### 5.7.2 Fissurectomy

Fissurectomy includes excision of the fibrotic edge of the fissure, curettage of its base, and excision of the sentinel pile and/or anal papilla, if present. Some groups consider it to be a more conservative treatment for anal fissure. It can be combined with

the application of BT [30] in an effort to improve the results, which are poorer when fissurectomy is done alone [31]. Published healing rates when combined with BT are between 70% [32] and 90% [30], and de novo incontinence is usually temporal and minimal (occurring in <5% of patients), or even absent in some other series [33].

### 5.7.3 Fissurotomy

Another novel procedure has recently been introduced in the surgical armamentarium for anal fissure: fissurotomy. It consists of unroofing the fissure, which significantly widens the distal anal canal, rendering internal sphincterotomy unnecessary [34]. Results have been promising, with less than a 2% recurrence rate and no change in continence status. More studies and longer follow-up are needed to support these findings, which could also be influenced by the amount of anal dilatation involved in the procedure.

### 5.7.4 Anal Advancement Flap (Flap Anoplasty)

Advancement flap procedures have been reported in the treatment of anal fissures. These procedures involve fashioning a local flap to cover the fissure defect. Different flaps have been reported: island flap [35], house flap [36], V-Y flap, and a rotational flap [37]. These procedures are combined with fissurectomy and/or BT application. They do not involve disruption of the IAS and are mostly performed in patients with anal fissures and either a high risk of incontinence or low-pressure fissures to avoid compromising continence even more. Reported healing rates are between 80% and 95%, with 7% flap disruption and a recurrence rate around 6%. The postoperative incontinence rate is less than 5% in the majority of reports [38, 39] (Fig. 5.8).

### 5.7.5 Anal Dilatation

Anal dilatation was one of the first surgical treatments for anal fissures. There are several ways to



**Fig. 5.8** Final aspect of the wound after a flap anoplasty for anal fissure (Courtesy of Dr. E. Garcia-Granero)

dilate the anus: manually, with progressive dilators, or with pneumatic balloons. Anal dilatation is not recommended as an outpatient treatment, neither under anesthesia nor under neuromuscular blockade. It does not show better results than other conservative treatments, is difficult and uncomfortable for the patient, and is related to an increase in incontinence (15–30%) [8]. The incontinence is caused by multiple instances of (uncontrolled) damage to the IAS.

Treatment with progressive pneumatic balloons seems to provide good initial results [7], but there is a need for more prospective studies before this is recommended as a standard treatment.

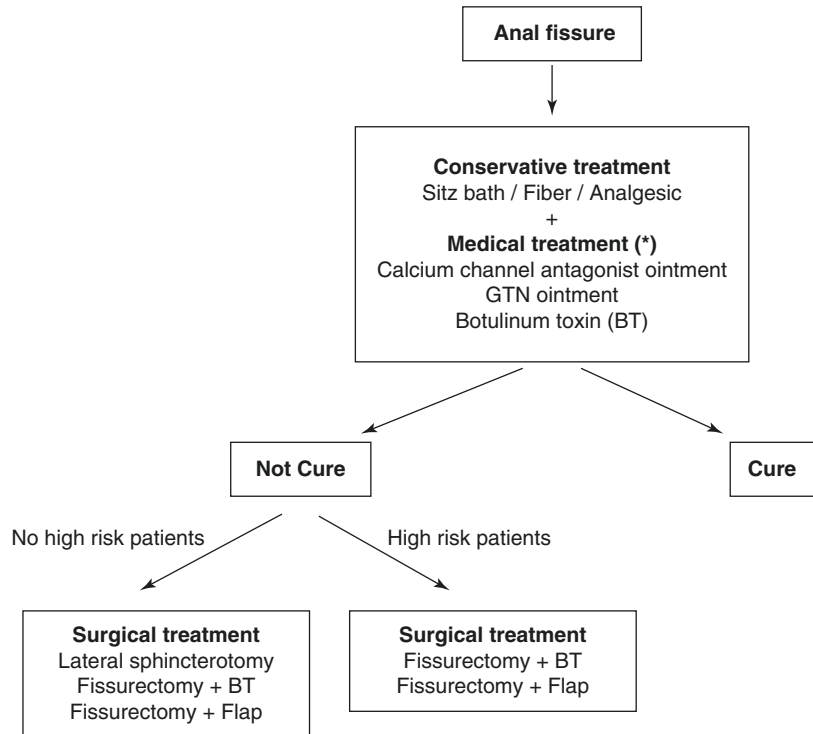
Fecal incontinence is without a doubt the main reason why pharmacological treatments have recently been replacing surgery as the initial treatment for anal fissure. Surgery has been compared with GTN, BT, and nifedipine. Although these studies show healing rates of 60–70% of patients treated with pharmacological and 95–97% of those treated with surgical measures, they conclude that drug therapy should be the first treatment option, especially in groups with a high risk for fecal incontinence (e.g., multiparity, previous anal surgery, radiotherapy), given the higher number of serious complications with surgery among them [6, 40–42].

### 5.7.6 Other Innovative Treatments

Other therapies are being tested for the treatment of chronic anal fissures, such as posterior



**Fig. 5.9** Proposed algorithm for anal fissure treatment



(\*) In high risk patients a second line of medical treatment if first line fails can be administered

perineal support devices [43], posterior tibial nerve stimulation [44], and sacral nerve stimulation [45]. More studies are needed to support the routine use, effectiveness, and cost analysis of these treatments in patients with anal fissure.

A basic algorithm for the treatment of anal fissure is proposed here (Fig. 5.9) according to the published evidence.

## 5.8 Complications

Complications of medical treatment of anal fissures are allergy to compounds, headache, and hypotension. These are usually dose dependent, easy to manage, and have minimal consequences for the patient.

The most important complication with all surgical techniques is the long-term consequence of permanently sectioning the sphincter: fecal incontinence. This condition can be temporary in up to 30% of operated patients and permanent in 3–13%

of patients [40]. Among operated patients, permanent incontinence after lateral sphincterotomy can result in flatus incontinence (9%), soiling/seeepage (6%), accidental defecation (0.91%), incontinence to liquid stool (0.67%), and incontinence to solid stool (0.83%). These percentages are affected by the procedure, the patient's characteristics, and the surgeon's experience. High-risk factors for postoperative incontinence include age [46], female sex (shorter anal canal) [40], vaginal deliveries [47], radiotherapy, and previous anal trauma.

## 5.9 Special Considerations

### 5.9.1 Low Tone/Incontinence

Patients with anal fissure and anal hypotonicity or fecal incontinence should be treated conservatively. If the initial treatment fails there are reports of treatment with an advancement flap [48]. This procedure does not involve excising

the anal sphincter and has shown excellent results in these kinds of patients, with more than 90% cure rates and no worsening of continence.

### 5.9.2 Recurrent Anal Fissure

A recurrent anal fissure can be a complex problem. Before starting treatment again, a complete evaluation of the symptoms and the aspect of the fissure, along with the patient's history and treatment preferences, is recommended [49].

Medical treatment should again be the first option, and a second line of treatment can be offered if the first fails. If this medical treatment does not cure the fissure, then surgery must be recommended (sphincterotomy, flap, fissurectomy with BT). If the patient already had a sphincterotomy, then a sphincter-saving procedure is encouraged (fissurectomy or flap).

### 5.9.3 Management of Concomitant Anal Lesions

Fibrous polyps and hypertrophied anal papillae are present in some chronic anal fissures and can be resected at the same time of sphincterotomy. However, adding a synchronous anal procedure (e.g., hemorrhoidectomy) at the time of sphincterotomy increases the risk of incontinence [47].

### 5.9.4 Crohn's Disease

Fissure in Crohn's disease is a common finding, although most of these fissures are related to the inflammatory disease and not to sphincter hypertonicity. Caution in treatment is mandatory. It is important to treat these patients accordingly, but it is also crucial to be as conservative as possible to avoid current or future complications. When medical treatment fails and there is no evidence of anorectal inflammation, a sphincterotomy has shown good results [50]. Multidisciplinary evaluation is highly recommended.

### 5.9.5 Anal Fissure in Children

Fissure in children should be treated with sitz baths and soft laxatives. If the fissure does not heal, then medical treatment should be tried: GTN or a calcium channel blocker ointments or BT administration are effective. Lateral sphincterotomy or fissurectomy are usually unnecessary and should be reserved only for those patients who do not heal with medical therapy alone.

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