#### ANAL FISSURE REVISITED: A SYSTEMATIC REVIEW

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**ABSTRACT:** Anal fissure is one of the most common anorectal problems. Anal fissure is largely associated with high anal sphincter pressures and most treatment options are based on reducing anal pressures. There are many options to treat chronic fissures in ano. Some of them are non-surgical while the others are surgical. The efficacy claimed by each of the prevalent method is very high but the inconsistencies and contraindications are equally strong. To date, lateral sphincterotomy has been favoured by most of the proctologists, because it is the least extensive surgical procedure and is offering a long lasting relief in sphincter spasm. Various management technique are reviewed in this article along with Advancement flap for anterior fissure and a new method combining the age-old technique of Lord's manual dilatation followed by radio surgery is also highlighted along with their complications. The addition of radio surgery is found useful for refreshing the edges of the fissure and to tackle pathologies namely sentinel pile, small internal piles or hypertrophied anal papillae often found associated with chronic fissures. Revisiting the trends of treatment of chronic anal fissures, the most preferred options are the manual dilatation with radio surgery and the subcutaneous lateral anal sphincterotomy. Both methods are easy to perform, have negligible complications and no special setup is needed, except the radio surgical unit, in case of the first procedure.

**KEYWORDS:** Fissure-in-ano, Sphincterotomy, Recurrence, Anal spasm.

**INTRODUCTION:** Fissure in ano is a troubling and painful condition that affects a great majority of the population world over. Anal fissure is the most common cause of severe anal pain. It is equally one of the most common reasons of bleeding per anus in infants and young children. It may be so severe that patients may avoid defecation for days together until it becomes inevitable. The fissures can be classified into 1] Acute or superficial and 2] Chronic fissure in ano. Approximately 90% of anal fissures in both men and women are located posteriorly in the midline. Anterior fissures occur in 10% of patients, more commonly women. Fewer than 1% of fissures are located off a midline position or are multiple in number. These atypical fissures may be associated with Crohn's disease, sexually transmitted diseases (Human immunodeficiency disease [HIV], syphilis, or herpes), anal cancer, or tuberculosis. Whereas acute fissures typically heal with medical management after 4 to 6 weeks, chronic fissures persist beyond 6 weeks. Chronic fissures are also associated with raised edges, exposed internal sphincter muscle, distal sentinel tag, and hypertrophied anal papilla at the internal apex.

Predisposing Factors: It has been proved that constipation is the primary and sole cause of initiation of a fissure1. Passage of hard stool, irregularity of diet, consumption of spicy and pungent food, faulty bowel habits, and lack of local hygiene can contribute for initiation of the pathology. In females, the ailment is usually triggered during pregnancy and following childbirth.

**PATHOGENESIS:** Despite extensive investigation of this disease, the exact etiology of anal fissure remains unclear. It appears that constipation with passage of hard stools or anal trauma may instigate

the fissure. However, in many instances patients do not report constipation or may have a history of watery diarrhea. Various studies have suggested that both anorectal mechanics and blood flow to the anal canal may play a role in anal fissure development. Initial reports from the 1970s and 1980s have implicated internal sphincter hypertonia in anal fissure pathogenesis.<sup>[1]</sup> More recent studies have used anorectal manometry to demonstrate hypertonia of the internal sphincter and have shown fewer internal anal sphincter relaxations in patients with chronic anal fissures.<sup>[2]</sup> In addition, relative ischemia of the posterior anal canal has been implicated in chronic, nonhealing anal fissures. Anal hypertonicity may aggravate perfusion to the anal canal.

Pressure on the vessels passing perpendicularly through the internal anal sphincter muscle during increased sphincter tone may compromise perfusion to the posterior commissure where blood flow is already sparse. The pathophysiology of anterior fissures may be different than chronic posterior fissures. Jenkins and colleagues showed that anterior fissure patients were significantly more likely to have occult external sphincter injury and impaired external sphincter function compared with posterior fissure patients. In addition, anterior fissures were identified in a younger and predominantly female group of patients. In these patients, maximum squeeze pressure was significantly lower compared with the posterior fissure group. Also, maximum resting pressure was not significantly elevated compared with controls, but was significantly elevated in posterior fissures. These findings may have important implications for the management and treatment of this common subgroup of anal fissure patients. [4]

**Treatment of Fissure in Ano:** The nature and anatomy of fissure in ano is quite clear, and much is known about the various predisposing and contributing factors that lead to initiation and progression of the disease. The preferred method of treating them, one that results in optimal clinical results and the least pain and inconvenience to the patient, however, has been open to debate.

Treatment of Superficial fissures: It has long been recognized that superficial fissures can be cured conservatively. The majority of initial anal fissures can be managed medically. In fact, almost half will heal with conservative therapy alone using warm baths and increased fiber intake. Warm sitz baths may lead to healing of anal fissures via a somatoanal reflex that results in relaxation of the internal anal sphincter. In a randomized study conducted by Jensen, treatment with 10g of unprocessed bran twice daily and warm sitz baths for 15 minutes twice daily and after each bowel movement resulted in quicker symptomatic relief and better healing at 3 weeks (88%) compared with 2% lignocaine ointment or 2% hydrocortisone cream. According to the practice parameters set by the American Society of Colon and Rectal Surgeons, increased fluid and fiber ingestion, the use of sitz baths, and if necessary, the use of stool softeners are safe, have few side effects, and should be the initial therapy for all patients with anal fissure.

When conservative measures fail, the next step in the management of anal fissure has traditionally been surgery.

Chronic or complicated fissure in ano: The above mentioned approaches do not prove effective in the chronic variety of fissures in ano. A definitive therapy is needed to tackle this stubborn malady. The fissure is labeled as chronic or complicated if it fulfils the following criteria.<sup>[3]</sup>

1. If not responding to conservative treatment. 2. If a fibrous anal polyp is present. 3. Presence of an external skin tag is noticed. 4. Presence of hemorrhoid is visible. 5. Induration is indicated at the edges of fissure. 6. If there is exposure of the fibers of the internal sphincter at the floor of the fissure. 7. The

base of fissure is infected. 8. A bridged fissure with underlying fistula [a post fissure fistula] is diagnosed.

It has been experienced that fissure, complicated by any of the above facts, neither heal spontaneously nor does it respond to conservative therapy.

**MATERIALS AND METHODS:** Various therapies advocated for treating these chronic fissures and which are presently in practice have been summed up in the following paragraphs. Reference are obtained from various journels and internet pub med. Such proven therapies may be grouped into nonoperative and operative maneuvers.

#### **Non-Operative Techniques:**

**1. Botulin Toxin**: Botulinum toxin is produced by Clostridium botulinum and acts as an inhibitory neurotransmitter preventing release of acetylcholine from the presynaptic terminals. It has been shown to cause relaxation of both the external and internal anal sphincters lasting for up to 3 months. [9] Jost and Schimrigk reported the first case of anal fissure treated with botulinum toxin in 1993. [10] Since then, there has been increased interest in the use of botulinum toxin injections for the treatment of anal fissures.

There have been various studies on dosing and location of injection of the botulinum toxin, but the most common location is directly into the internal anal sphincter on either side of midline. [11][12] Retrograde endoscopic delivery of BOTOX® (Allergan, Inc., Irvine, CA) into the internal anal sphincter has also been described as being more accurate and better tolerated by patients in one group. [12] The value of this dosing regime awaits validation. Doses have varied between 5 to 100 units of BOTOX®, with various studies suggesting a dose-dependent efficacy of BOTOX® treatment. [13][14]

Compared with placebo, injection of botulinum toxin into the internal anal sphincter has been shown to be significantly better at healing anal fissures (73%) and in symptomatic relief (87%) at 2-month follow up. $^{[15]}$  Various randomized prospective studies have compared botulinum toxin injection with glyceryl trinitrate for the treatment of chronic anal fissures. According to a meta-analysis of 180 patients included in these studies, botulinum toxin and glyceryl trinitrate had equal healing rates, but glyceryl trinitrate had higher side effects and headaches. $^{[16]}$  In another prospective study, overall cure rates between nitroglycerine ointment, diltiazem ointment, and botulinum toxin injection were similar at 54%, 53%, and 51%, respectively. $^{[17]}$  Overall recurrence of anal fissure with botulinum toxin therapy is common (up to 55%), but retreatment with a higher dose may be effective. $^{[13][18]}$ 

The main side effect with botulinum toxin injection is mild incontinence to flatus and stool, lasting up to 3 weeks. [18] Although the risk is significantly lower compared with lateral internal sphincterotomy, there have been two case reports of long-term fecal incontinence with botulinum toxin injection of the anal canal. [19] In a randomized controlled trial by Arroyo and colleagues, one-year healing with botulinum toxin injection was 45% versus 93% with lateral internal sphincterotomy. Fissure recurrence was 55% within one year compared with 8% with lateral internal sphincterotomy. [20] One single-center, retrospective study found that the use of botulinum toxin injection helped prevent surgery in 73% of patients who presented with anal fissure in 2004 compared with patients in 1993 when sphincterotomy was first-line therapy. [21] Thus, botulinum toxin injection offers reasonable success with minimal side effects and is a reasonable option for "chemical sphincterotomy" in the management of chronic anal fissure.

Yet, the question remains as to whether botulinum toxin injection can be used when other medical therapy has failed. Two prospective randomized trials evaluating patients with chronic anal fissures that have failed previous pharmacologic management showed poor healing rates (As low as 27%) with subsequent botulinum injection therapy. The use of botulinum toxin injection for treatment of recurrent anal fissure after lateral internal sphincterotomy has been investigated, but the study was flawed with an extremely high incidence of recurrent anal fissures after sphincterotomy. [22][23] The toxicity of the drug, accidental injection in the surrounding tissue amounting to general poisoning, haematoma and infection reported had discouraged regular use of this therapy.

- 2. Calcium Channel Blocker: Calcium channel blockers (CCBs) relax the internal anal sphincter by blocking the influx of calcium into the cytoplasm of smooth muscle cell. It has been shown that both nifedipine (0.2–0.5% gel) and diltiazem (2% cream) promote fissure healing by decreasing mean anal resting pressure. [24][25] Topical CCBs have been shown to be better than both lignocaine ointment and hydrocortisone cream, with up to 95% remission in two studies. [25][26] Compared with GTN, topical application of CCBs has been shown to be equally effective with fewer side effects in various prospective, randomized studies. The principal side effect is mild headache, seen in up to 25% of patients. [26] Topical nifedipine has also been compared with lateral internal sphincterotomy with healing rates of 97% and 100% at 8 weeks. Long-term follow up at 19 months showed healing rates of 93% and 100% for the nifedipine and lateral internal sphincterotomy (LIS) groups, respectively. [27] On the other hand, oral calcium channel blockers have been shown to have poor healing rates (< 20% at 4 weeks in one study), high side-effect profile, and high therapeutic dropout. [25] Thus, with reasonable healing potential and minimal risk to the patient, topical CCBs are an acceptable choice for the medical management of chronic anal fissure.
- **3. Topical Nitrates:** Organic nitrates such as glyceryl trinitrate (GTN) undergo cellular metabolism to release nitric oxide (NO). Nitric oxide works as an inhibitory neurotransmitter in the internal anal sphincter resulting in sphincter relaxation. The topical application of GTN in dilute form (0.2%) has been shown to cause decreased anal resting pressures. Various studies have since emerged to investigate the use of GTN to treat anal fissures. In a Cochrane Review of 53 randomized controlled trials (RCTs) of nonsurgical therapies for anal fissures and 15 RCTs that specifically looked at GTN versus placebo, GTN was found to be marginally but significantly better than placebo in healing anal fissures (49% vs 37%, p<0.004). However, late recurrence was shown to be common (>50%) in those initially cured. In addition, dose made no difference in healing of anal fissures in three studies that compared doses of GTN ranging from 0.05% to 0.4% GTN. The key drawback, however, to GTN therapy is the high incidence of side effects, primarily headaches and light-headedness. In fact, up to 20% of patients cease GTN therapy due to the severity of their headaches.

A 2%GTN ointment applied twice to the anoderm for 6 weeks results in a complete healing in 98% of patients.<sup>[6]</sup>

In another study, Topical diltiazem ointment was used as an agent for chemical sphincterotomy for chronic anal fissure. The Study claims to offer significant healing rate and reduced incidences of side effects.<sup>[7]</sup>

However, during the course of therapy, strict dietary restrictions to smoothen the stool are necessary. Headache during therapy is a major concern with the incidence as high as 20–100%. Though the application of GTN has a high healing rate; it also has a high recurrence rate.

**4. Direct Current Probe Treatment:** This method is tried in patients of chronic anal fissures with associated internal hemorrhoids.

A study claimed that when the DC probe [Ultroid, Homeron] was applied to the internal hemorrhoids, the patients were relieved of anal pain and healing occurred in 90% of patients. [34] However, this mode of treatment requires special equipment and the procedure takes a very long time to be performed [About 10minutes for each hemorrhoid]. Moreover, the mechanism of action on the part of fissure is also not understood. A case of complication in the form of perianal abscess and fistula requiring surgery has been reported following DC probe treatment. [35]

**5. Endoscopic Anal Dilatation**: In this procedure, anal dilatation is performed with a two-valved anoscope under local anesthesia as an office procedure.<sup>[36]</sup>

In the study, 93% patients were found symptom free one month after the procedure, and only a few had a recurrence.

This procedure is said to be free of discharge or defect of continence either transient or permanent. In another series, a Parks' retractor or a recto sigmoid balloon has been used for sphincter dilatation. Out of 495 patients treated through this procedure, it is reported that in as many as 87–88% of the patients, the fissures were healed within 3 months.<sup>[37]</sup>

As many references are not available in support of this technique, it will be hazardous to comment on the efficacy or otherwise of this procedure.

**6. Unproven Therapies:** The internal anal sphincter is stimulated by  $\alpha 1$ -adrenergic innervation and is inhibited by cholinergic innervation by the sacral parasympathetic fibers. Topical bethanechol, a muscarinic agonist, has been shown to cause a dose-dependent reduction of anal pressure, with a maximal 24% reduction seen with 0.1% bethanechol. Although this data appears promising, large, prospective studies are needed before any treatment recommendations can be done.

**OPERATIVE INTERVENTION:** When conservative measures fail, a surgical approach becomes necessary for the definitive management of the chronic anal fissure.

**1. Stretching of Anal Sphincter [Lord's Anal Dilatation]**: Dilation of the anal canal for the treatment of anal fissure was first described in the 1860s, but was popularized in the 1960s. In 1964, Watts and colleagues reported on 99 patients with anal fissures treated with anal stretch. They describe the procedure as a manual stretching of the anal canal with two, then four fingers applying considerable outward force on the lateral walls of the anal canal. Dilation is performed for no less than 4 minutes. They reported satisfactory early relief of symptoms in 95% of patients, with fissure recurrence noted in 16% of patients.<sup>[39]</sup>

However, recent studies have shown that anal dilation has a higher risk of fissure persistence and higher risk of incontinence. [30], anal stretch has been scrutinized for causing extensive damage to internal and external sphincters leading to incontinence. A recent randomized controlled trial enrolled 108 patients assigned to anal dilation (AD) versus left lateral sphincterotomy (LLS). Average follow-up was 11.2 months. Significantly more patients reported minor incontinence in the AD than in the LLS group. Recurrence occurred in 11% of AD patients versus 2% of LLS patients [40] In addition, a Cochrane Review of seven randomized controlled trials, comparing anal stretch with internal sphincterotomy significantly favored sphincterotomy over anal stretch for efficacy (OR=3.35; 95% CI= 1.55–7.26) and

incontinence to flatus or feces (OR=4.03; 95% CI=2.04–7.46).[41] Although the procedure in itself is curative, in cases with associated pathologies, it has to be supplemented with an additional procedure.

- **2. Pneumatic Balloon Dilation:** In an effort to standardize the method of anal dilation, pneumatic balloon dilation (PBD) has been developed. Sohn and colleagues first described PBD using a 40-mm rectosigmoid balloon. A recent randomized controlled trial looked at PBD rather than manual dilation in comparison to lateral internal sphincterotomy (LIS) for the treatment of chronic anal fissure. Pneumatic dilation was performed with a 40-mm diameter by 60-mm-long anal balloon (Microvasive, Genova, Italy) with the balloon inflated to 20 psi for 6 minutes. Overall healing rates at 6 weeks were 83 and 92% for PBD and LIS, respectively. Based on preoperative and postoperative manometry, both techniques reduced anal pressures by  $\sim$ 30%. The PBD group did demonstrate mild transient fecal incontinence; however, at 24-month follow-up, the incidence of incontinence in the PBD group was 0%, but 16% in the LIS group (p<0.0001). Thus, with a better ability to standardize the technique and produce reproducible results, pneumatic balloon dilation may become a preferable alternative to anal dilation.
- **3. Division of Internal Anal Sphincter:** Division of internal sphincter fibers to relieve the sphincter spasm is presently considered the preferred therapy for chronic, recurrent and non-healing fissures.<sup>[31]</sup>

Nonetheless, lateral internal sphincterotomy still stands as the surgical treatment of choice for refractory anal fissures and may be offered without pharmacologic treatment failure according to the practice parameters by the American Society of Colon and Rectal Surgeons. [8] Reports of sphincterotomy for various anal pathologies probably date back to the 1700s. However, internal sphincterotomy for the management of anal fissure was first described and popularized in the 1950s by Eisenhammer. Lateral internal sphincterotomy quickly gained recognition as the posterior approach was found to result in large wounds and incontinence due to a "key-hole deformity." Lateral internal sphincterotomy is performed with a radial incision in the anoderm laterally exposing the internal sphincter muscle fibers. Then, under direct vision, the distal 4/5th of the internal sphincter muscle is divided with a scalpel or scissors. The wound can be left open or closed primarily. In 1969, Notaras described a technique that he called lateral subcutaneous sphincterotomy, now also known as a closed lateral internal sphincterotomy.

This resulted in even smaller wounds and fecal soiling rates dropped to 6% compared with 30–41% with a posterior internal sphincterotomy. This technique involves a narrow-bladed scalpel such as a cataract knife introduced through the perianal skin on the lateral side and pushed subcutaneously upwards between the internal sphincter and the skin lining the anal canal. When the point of the blade is at the dentate line the internal sphincter is divided by cutting medial to lateral. A defect can be felt under the skin between the retracted edged of the internal sphincter. A second approach for closed lateral internal sphincterotomy is the lateral to medial approach. In this operation, the scalpel is inserted into the intersphincteric groove and directed up to the dentate line. At this point, the internal sphincter is divided, cutting laterally to medially toward the surgeon's finger in the anal canal. [46],[47]

Since the 1950s and 1960s, numerous studies have evaluated different methods of sphincterotomy. Various randomized controlled trials have compared open versus closed techniques. Healing rates appear to be similar, with open techniques ranging from 93% to 95% and closed approaches ranging from 90% to 97%. There appears to be no difference in major incontinence rates,

which range from 2% to 5%. When comparing lateral internal sphincterotomy with midline posterior sphincterotomy, again there appears to be no significant difference in persistence of symptoms or incontinence in two meta-analyses of retrospective studies.<sup>[48],[49]</sup>

Since the description of the technique of lateral internal sphincterotomy by Eisenhammer in the 1950s, [44] current practice remains that the division of the internal sphincter be taken to the dentate line. However, with high reports of incontinence with LIS, there has been a more prudent approach to division of the sphincter that may yield lower incontinence rates. Littlejohn and colleagues described a technique of tailored left lateral sphincterotomy, wherein the sphincter is divided up to the height of the fissure. They showed a 99% initial healing rate, 0.7% incidence of urgency, 1% gas incontinence, and 35% minor staining. [50] However, this comes with a higher overall treatment failure rate on long-term follow-up (13%) compared with a larger sphincterotomy either to the dentate line (0%) or to an anal diameter of 30mm (3%). [51], [52] Thus, a traditional, longer sphincterotomy, with fewer treatment failures and an acceptable rate of mild incontinence, appears to be the preferred technique.

Complications associated with lateral internal sphincterotomy are incontinence, ecchymosis, hematoma, and wound infection. In the past, there has been fear that closure of these wounds would result in a higher complication rate, such as wound infection. Two prospective, randomized studies compared primary closure of the wound after LIS with leaving the wound open to heal secondarily. In the study by Aysan and colleagues, there was a significantly faster healing rate of 15.05±5.60 days with wound closure versus 33.94±6.67 days when wounds were left open (p<0.001).<sup>[53]</sup> In a combined analysis, the advantage of closure was not statistically significance (p=0.35, 95% CI: 0.13–1.00).<sup>[41]</sup>

**4. Advancement Flap Surgery:** The management of anal fissure largely relies on relieving anal hypertonicity. Patients with anterior anal fissures have been shown to have significantly lower anal pressures, suggesting a different pathophysiology in the development of these fissures.<sup>[4]</sup> In support of this idea, there have also been reports of a paradoxical contraction response of low-pressure fissures to treatment with botulinum toxin.<sup>[22]</sup> These patients are at particularly high risk for incontinence with measures directed at reducing anal hypertonia. Various small studies have shown success with advancement anoplasty, or fissurectomy with advancement anoplasty, in patients with low-pressure anal fissures with success rates ranging from 87% to 100%.<sup>[54],[55]</sup> Advancement flap surgery may be an acceptable first approach to low-pressure fissures.

Various studies have also evaluated advancement flap surgery for all chronic anal fissure types. The procedure typically involves a subcutaneous flap with an incision made from the anal verge extending caudally. The skin flap is then advanced into the anal canal and positioned to cover the anal fissure and sutured in place. Two independent studies showed 98% success rate with advancement anoplasty for the treatment of chronic anal fissure, irrespective of anal tone. [56],[57] In a recent pilot study of 8 patients, autologous adipose tissue transplant has also shown 75% healing of anal fissure and 80% resolution of anal stenosis in patients with chronic anal fissure who failed previous medical and surgical therapy. [58] Although these studies have shown promising results, larger prospective studies and longer follow-up is needed before further recommendations can be made in comparison to lateral internal sphincterotomy.

**5. Combined Outpatient Surgical and Cyrotherapeutical Treatment:** A lateral anal sphincterotomy, which is done under local anesthesia, is followed by fissure curettage with N protosside cryosound. [59] This is claimed to be quicker and more effective procedure.

**6. Carbon Dioxide Laser Surgery:** It involves laser vaporization of the fissure locally. The internal sphincter can be incised using this laser. In long-standing fissures, some degree of anal stenosis is present. It can be used to give relieving incisions in the three quadrants other than the fissure before the fissure is attended. The high cost of the laser unit seems to be the major deterrent in its wider acceptance.

**7. Lateral Subcutaneous Internal Sphincterotomy and Radio Frequency Surgery:** In an attempt to improve on the available options, a fusion of method of sphincterotomy with radiofrequency is described. The procedure has been claimed to be effective in cases where the fissure is associated with pathologies like sentinel tags, hypertrophied anal papillae, fibrous polyps, post fissure fistula or internal hemorrhoids which can be tackled simultaneously while the fissure is being treated. [30], [31] The radio frequency surgical unit used is Ellman Dual Frequency 4MHz by Ellman International [Hewlett, NY], which incorporates threefold function of cutting, cutting and coagulation or pure coagulation. It is claimed that the edges of the fibrosed fissure can be refashioned with the help of the radio frequency surgery. The entire procedure is quick and is virtually bloodless. [60]

Being a new introduction with no controlled or randomized trials available, this treatment modality needs further studies to analyze long-term results.

**CONCLUSION:** Anal fissure is a common problem. The pathophysiology is based on high sphincter pressures and management is generally aimed toward reducing anal pressures. Anal fissures can generally be treated with conservative management, but pharmacologic management with topical calcium channel blockers, topical nitrates, and botulinum toxin injection are reasonable options with minimal side effects and good cure rates. Lateral internal sphincterotomy remains the gold standard for definitive management of anal fissures, but comes with a risk of incontinence. Open or closed techniques can be used with similar healing and complication rates. Anal stretch should be abandoned in the management of anal fissure.

Larger studies with longer follow-up are needed before recommendations can be made about various other treatment modalities for anal fissure. Particular attention must be paid to anterior anal fissures as they are typically associated with low anal pressures. These patients should undergo anorectal manometery testing preoperatively. Those patients with sphincter hypotonia who fail conservative management should undergo advancement anoplasty. However, recent data suggests that lateral internal sphincterotomy may be tolerated well in these patients when conservative management fails.

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