Review Article

DOI: 10.5455/2349-2902.isj20150502

Surgical management and therapeutic prospectus of anal fistula: a review

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Received: 22 January 2015 Revised: 26 January 2015

Accepted: 06 February 2015

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ABSTRACT

A fissure in ano is a tear in the anoderm distal to the dentate line. The pathophysiology of anal fissure is thought to be related to trauma to the anoderm from any cause. A tear in the anoderm causes acute pain, which results in spasm of the internal anal sphincter and decreased blood supply to the anoderm. This cycle of pain, spasm and ischemia contributes to development of a poorly healing wound that becomes a chronic fissure. In this review article our aim to discuss the surgical management and therapeutic prospectus of anal fistula.

Keywords: Fissure, Anoderm, Therapeutic

INTRODUCTION

Anal fistula (AF) is a communication between the anorectal canal and the perianal skin that is lined with granulation tissue. It may be useful to consider it as a tunnel during discussions with patients. The fistula may harbor chronic infection, which may discharge continuously or intermittently through the opening on to the skin. Intermittent discharge is usually caused by cyclical accumulation of an abscess with associated discomfort and pain before some relief from discharge, which is followed by further accumulation. In the most severe cases, faecal material may also pass through the tunnel and cause soiling of underwear and skin irritation. The prevalence of anal fistula is per 10,000 of the population in European studies, but this is probably an

underestimate, with many patients being reluctant to present to medical services. 1,2

ANATOMY

An understanding of the anatomy of the anal canal is essential for the appropriate management of anal fistulas. The external sphincter (ES) is a continuation of the pelvic floor musculature. The internal sphincter (IS) is a continuation of the inner circular muscle layer of the lower rectum. These muscle layers are easily appreciated on endo-anal ultrasound (EUS). The IS appears as a hypo-echoic ring. The ES is identified by first identifying the puborectalis sling at the ano-rectal junction. This is hyper-echoic and U-shaped. Below this the ES commences when the open end of the U begins to close

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to form a complete ring of muscle.³⁻⁶ The mucocutaneous junction is the site of the dentate line (the term pectinate line should be discarded).⁷ The epithelium of the anal canal is mucosa above the dentate line and stratified non-keratinized squamous epithelium below. The dentate line is the site of the anal valves. Proximal to each anal valve is an anal crypt or sinus, which macroscopically appears as a small pit. The anal glands, which lie in the intersphincteric plane, empty into these anal crypts. For a distance of 5–20 mm (varying with age) above the dentate line, the mucosa is cuboidal and is known as the anal transitional zone (ATZ).^{8,9} This area is thought to be important for discrimination between flatus and faeces.

ETIOLOGY AND PATHOGENESIS

Most (~90% in most case series) anal fistulas are idiopathic.^{1,3} Infection of glands in the intersphincteric space of the anal canal is thought to underlie both acute anorectal abscesses and anal fistulas the "cryptoglandular hypothesis." The exact cause or mechanism of infection has not been fully elucidated, but it spreads through pathways of least resistance, and in so doing creates a track that persists thereafter. Hence, a common presentation is an acute abscess that fails to heal after surgical drainage or recurs at the same site. It is not clear why certain cases of perianal sepsis are limited to abscess formation whereas others are associated with fistula formation. It is widely accepted that adequate surgical drainage is the optimal treatment for acute abscesses and that antibiotics are indicated only for treatment of surrounding cellulitis. A recent review of perianal abscess and fistula quotes a fistula formation rate of 26-37% after perianal abscess. 10 Microbiological culture of pus from an adequately drained abscess may help to predict fistula formation. Small case series have shown that the abscess is unlikely to recur or develop into a fistula if only skin organisms are grown (0-30% of cases in most studies). 11,12 When gut organisms are cultured, most studies have shown that 80% or more abscesses have an underlying fistula. Some cases of anal fistula will be associated with other condition such as Crohn's disease, tuberculosis, hidradenitis suppurativa, and previous surgery or radiotherapy (box). Cancer may present as a fistula or arise within a chronic complex fistula. Fistula arising from ano-rectal or obstetric trauma may be prevented if the wound is carefully debrided and repaired at the time of injury.

THERAPEUTIC MANAGEMENT

Smooth muscle relaxation is an effective treatment for AF and has advantages over surgical treatment in avoiding long term complications. Additionally, it does not require hospitalization. ^{13,14}.

Glyceryl trinitrate (GTN): Topical GTN, a nitric oxide donor compound, has been shown to cause relaxation of the anal sphincter. It has been reported that blood flow at the posterior midline of anoderm is inversely related to

the mean maximum anal resting pressure and topical application of GTN ointment increases the blood flow to posterior midline.¹⁵

Calcium channel blocker

Diltiazem (DTZ): The internal anal sphincter has a calcium-dependent mechanism to maintain tone and also receives inhibitory extrinsic cholinergic innervations. It may therefore be possible to lower anal sphincter pressure using calcium channel blockers and cholinergic agonists without side effects. Griffin et al. used topical DTZ ointments to heal patients with CAF that had failed previous treatment with topical GTN (0.2%). Patients (N=47) with CAF who had previously failed at least one course of topical GTN were recruited prospectively from a single center. They applied DTZ (700 mg of 2%) cream to the anal verge twice daily for 8 weeks. Forty-four percent of patients who completed treatment were cured of fissures. Another 42% of patients with persistent fissures were symptomatically improved. Thus surgery could be avoided in 70% of patients. 16

Nifedipine (NIF): NIF has also been used in treatment of AFs as reported in a number of studies. ¹⁷ In a prospective, randomized, double blind, multicenter study, the efficacy of local application of NIF ointment (0.2%) in healing acute AF was determined. Patients (N=141) applied topical NIF ointment every 12 h for 3 weeks. The control group (N=142) received topical lidocaine (1%) and hydrocortisone acetate (1%) ointment during therapy. Manometry was performed before and after 14 and 21 days. After 21 days of therapy, 95% and 50% of patients were healed in the NIF group and control group, respectively (p <0.01). A mean reduction of 30% (p <0.01) and 188.8% (p<0.01) in anal pressure and squeeze pressure was observed.

Lacidipine: Lacidipine is a calcium channel blocker like nifedipine and hence finds its use in the treatment of AFs. Twenty-one consecutive patients (16 women) with AF (16 chronic, situated posteriorly in 17 patients, anteriorly in 4 patients) with a mean age of 37.1 yr. were treated with oral lacidipine (6 mg daily). Blood pressure, pain scores (assessed from 0 to 10 on a visual analogue scale), and fissure healing were monitored after 2, 4, and 8 weeks. However, about 33.3% patients developed side effects. Pain scores were significantly reduced after 2 weeks and continued to show a significant reduction throughout the treatment period. Fourteen percent and 90.4% of fissures were healed after 14 and 28 days, respectively. No recurrences in fissures were reported.

Gonyautoxin: All the above treatments mentioned for AF, viz., LIS, GTN, LA, NIF, and BTX, focused on reducing the tone of the internal anal sphincter. In a recent publication, Garrido and colleagues have described the successful use of a new agent, gonyautoxin, in patients with acute AF and CAF. ¹⁹ Gonyautoxin is a paralyzing phytotoxin produced by dinoflaointmentlates.

It breaks the vicious circle of pain and spasm that leads to AF. Fifty recruited patients received clinical examination, including proctoscopy and questionnaire to evaluate the symptoms. 20 Anal manometry was performed before and after Gonyautoxin (100 U/mL) injection into both sides of the AF in the internal anal sphincter. Total remission of acute AF and CAF was achieved within 15 and 28 days, respectively. Ninety-eight percent of the patients healed before 28 days with a mean time healing of 17.6±9 days. Only one relapsed during 14 months of follow-up. There was about a 56% decrease in resting pressure when compared with baseline. No side effects were observed.

Isosorbides

Isosorbide mononitrate (ISM): Tankova et al. conducted a study to assess the efficacy and patient compliance of topical mononitrate hydrocintment for the treatment of AF. ISM (0.2%) was applied to the anal canal twice daily for 3 weeks. Anal pressure was determined using anal manometry before and after the therapy. At the end of therapy, 88% and 22% fissures were healed in treated and control group patients, respectively. Twenty percent of patients suffered from mild heart attack. No fecal incontinence and recurrence occurred during 3 months of follow-up.

Isosorbide dinitrate (ISDN): In a randomized, prospective, double-blind, placebo controlled trial, 37 consecutive subjects with AF were enrolled.²¹ The subjects were divided into two groups. One group (N=20) received ISDN and the other group (N=17) was given placebo. Both groups were treated for a median of 5 weeks. After this period, 17 subjects in the isosorbide group had healed compared with 6 controls (p <0.003). The fissure recurred in 2 patients who had an initial good response to isosorbide, and in 2 patients of the control group. Side effects (particularly headache) were more common after ISDN.

In a study carried out by Songun et al., patients (N=100) with AF were treated with ISDN, the primary healing rate of AFs was 93% with ISDN.²² In case of recurrence (13%), 54% could again be treated successfully with ISDN, but a complication (temporary headache) was observed in about 7% of patients.

L-arginine (LA)

Nitric oxide produced from the cellular metabolism of LA also causes relaxation of the internal anal sphincter. A study investigated by Griffin et al. reported that topical LA can be used as a possible alternative treatment for CAF. 23 In a two-center study, volunteers (N=25) received LA (400 mg) or placebo. Anal manometry was performed 2 hours after application of LA ointment or placebo ointment. It was found that LA ointment significantly lowered MRAP. LA ointment had a rapid onset of action with a duration of action of more than 2 h (p <0.01).

Minoxidil and Lignocaine

In a prospective, randomized, double-blind study, 90 patients with AF were recruited. Patients received local applications of ointments containing 5% lignocaine (N=28), 0.5% minoxidil (N=36), or both (N=26). Healing of AF at 6 weeks was considered as the primary end point. The healing rate was similar in the three groups. However, the mean time taken for complete healing with combination treatment (1.9 weeks) was significantly shorter than that with minoxidil alone (3.1 weeks, p =0.001) or with lignocaine alone (3.3 weeks, p =0.002). Thus, a combination of minoxidil and lignocaine helped in faster healing of AF and provided better symptomatic relief than either drug alone.

SURGICAL MANAGEMENT

The objectives of management have been outlined by Finlay:²⁵

- 1. To define the anatomy of the fistula
- 2. To drain any associated sepsis
- 3. To eradicate the fistula track
- 4. To prevent recurrence
- 5. To preserve continence and sphincter

After full assessment, it is the author's practice to either lay open the fistula or place a seton and then re-assess after 2–3 months. At this time the fistula may now be able to be laid open or a rectal advancement flap can be performed.

In the past, anal fistulas were treated by laying open the fistula tract (fistulotomy), a method that may have been used at least as long ago as the classical Roman era. Most practitioners preferred to open the tract widely enough so that the anal end of the fistula healed first. However, the more the anal sphincter is involved in the fistula, the greater the chance that surgical treatment will cause fecal incontinence. Because of this risk, surgeons began to use a silk ligature (seton), which was passed through the sphincter with the idea that the presence of the device would promote healing. There are two types of setons. A cutting seton is tied tightly and replaced with another tied seton when it loosens as the body extrudes it (a "slow fistulotomy"). A loose seton is placed only to facilitate drainage, thereby helping to control infection. Setononly therapy for anal fistulas is still used in some cases, but healing may take months and the treatment is associated with considerable pain, scarring of the perianal tissues, and fecal incontinence rates of up to 67%.26 Another alternative for treating anal fistulas is creation of an anal mucosal flap. Various types of flaps have been used, including tongue flaps, lip flaps, and tubular or sleeve flaps. The goal of all flap treatments is to cover the internal fistulous opening, blocking passage of fecal material into the fistula so that the tract can heal. Initially, secondary necrosis of flaps, with consequent reopening of the fistula, was common. To prevent necrosis, some surgeons cut into the internal sphincter, hoping that this would help maintain blood supply to the flap. However, the more the sphincter muscle is used as a flap, the higher the risk of fecal incontinence. Although healing rates in patients treated with a mucosal flap may be as high as 70%,³ fecal incontinence rates have exceeded 25% in several series. Recently, various sphincter-sparing techniques for treating anal fistulas have been developed with the aim of avoiding fecal incontinence. The first was instillation of fibrin glue, which was initially made at operation by the surgeon from the patient's own blood but is now available commercially. Fibrin-glue treatment preserves continence, and the early experience with this method indicated that it was effective in achieving healing. However, as the procedure gained wide acceptance, success rates began to decrease, especially in patients with complex fistulas. Although success rates ranging from 14% to 74% have been reported,8 the average is about 30% to 50%. 27,28

The next sphincter-sparing method introduced was implantation of a collagen anal fistula plug (Surgisis® Cook Medical, Bloomington, IN), a device composed of lyophilized, decellularized porcine small-intestinal submucosa. We began to use this plug in 2007 and gained a good deal of experience with it. We found that it had certain faults, however, with the most important being a tendency to fall out, sometimes on the day of implantation or a few weeks later. Indeed, collagen-plug extrusion rates of about 20% or higher have been observed in a number of studies, 29-32 including at least one randomized trial.³³ In another randomized trial, the fistula recurrence rate after implantation of a collagen plug was 71%.34 The next sphincter-sparing innovation was the GORE® BIO-A® Fistula Plug, which was introduced into the US market in 2009. This plug is a completely synthetic prosthesis composed of polymers (polyglycolic acid/ trimethylene carbonate [PGA/TMC]) that are gradually absorbed by the body. The PGA/TMC material has a three-dimensional matrix of open, interconnected pores that serves as a scaffold for tissue regeneration. The plug device consists of a disk to which three pairs of tubes or "legs" (a total of six) are attached. By removing one or more of the legs, the surgeon can tailor the plug to fit and fill a specific fistula, thereby possibly decreasing he likelihood of plug dislodgement and treatment failure. In a nonrandomized comparative study, the synthetic plug had a success rate that was more than four times higher than that of the collagen plug.³⁵

CONCLUSION

Medicinal treatment has advantages over surgical treatment in avoiding long term complications. New formulation and combination of GTN will be beneficial in treatment of anal fissure due to fewer side effects.

Funding: No funding sources Conflict of interest: None declared Ethical approval: Not required

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DOI: 10.5455/2349-2902.isj20150502 **Cite this article as:** Aggarwal V, Dhingra R, Singh G, Monga S, Jain A, Bansal V et al. Surgical management and therapeutic prospectus of anal fistula: a review. Int Surg J 2015;2:125-9.