Review Article

Current concept of pathophysiology and Biochemical factors involved in acute and chronic anal fissure

Amrut Dambal, Samata Padaki[1], B. Kusuma Kumari[1], K. Kesava Ram[1], Anand Hugar[1], K, Harika Priyadarshini[1], Noorjehan Begum[1]

Department of Biochemistry,[1]Department of Physiology, Mallareddy Institute of Medical Sciences, Hyderabad, Andra Pradesh, India.

Abstract

Anal fissure is one of the most common causes of severe anal pain. Factors which predispose people to develop anal fissure include diarrhea, constipation, childbirth, medication as well as constant saddle vibration (amongst professional mountain-bikers) and using a jet of water from a bidet-toilet. For many years, it has been generally accepted that a sphincterotomy, whether surgical or pharmacological, treats chronic anal fissure as it produces a reduction in anal pressure, reverses sphincter spasms and promotes fissure healing. However, recent studies cast doubt upon this explanation. A new theory explains that anal fissure healing depends on biochemical processes taking place in the anal passage. Eruption of tissues in the fissure region during defecation releases platelet products such as ADP, ATP, 5-HT, platelet activation factor, thrombin and substance P which cause the contraction of smooth muscles (of Internal Anal Sphincter and blood vessels) and results in difficulties in fissure healing. Reducing trauma of defecation by posterior perineal support plays an important role in anal fissure healing. It brings a significant improvement in the symptoms of patients with anal fissure.

Key Words: Anal fissure, ischaemia, anal pressure, anal sphincters, anorectal manometry,

Introduction

An anal fissure is a linear, longitudinal tear or ulcer extending below the dentate line to the margin of the anus. They are a common condition in this area of the body. They will cause pain during bowel movements which can often become extremely severe and painful. Exact incidence of anal fissure is unknown. Patients suffering from anal fissure make up 10-15% of all proctologic consultations [1,2,3,4] and it affects all age groups with an equal incidence in both sexes [5]. On an average, 2,35,000 new cases of anal fissure are reported every year in the USA and about 40% of them persist for months or years [6].

PATHOPHYSIOLOGY OF ACUTE AND CHRONIC ANAL FISSURE

Fissures may be caused due to trauma, due to hard stool or diarrhea, or insertion of items into the anus (such as rectal thermometers, enema or an endoscope), or a tear to the perineum during childbirth. These primary anal fissures are most commonly located in the dorsal part of the anus in 85% cases. Constant saddle vibration in professional mountain bikers can lead to micro trauma and chronic inflammation which may result in anal fissure [7]. It is believed that the water stream in a bidet-toilet could be a cause of anterior fissure-in-ano [8].

Address for Correspondence
Dr. Amrut Dambal, Assistant Professor, Department of Biochemistry
Mallareddy Institute of Medical Sciences, Hyderabad-55, Andra Pradesh, India.
E-mail:-amrutdambal@yahoo.com

If the fissure does not occur in this area then there may be another underlying cause. This can include anal cancer, leukaemia, Crohn's disease, viral infections, tuberculosis, gonorrhoea, chlamydia, human immunodeficiency virus (HIV), and traumatic injuries (sexual, iatrogenic). 10% of ventral fissures frequently occur in women and 5% are lateral fissures.

Fissures may be classified as acute or chronic. Acute fissures are superficial and heal in more than 50% cases spontaneously or after treatment whereas chronic fissures are profound, seen 4-6 weeks after initial lesion and do not heal spontaneously.

On physical examination, an acute fissure will appear to be a mere crack in the epithelium, typically beginning at the anal verge and traveling proximally along the anal canal toward the dentate line. Over time, a number of factors occur precipitating the well-known secondary clinical features of a chronic fissure. The distal epithelium can become edematous and fibrotic resulting in a sentinel tag or pile at the distal margin, often indistinguishable from a typical hemorrhoidal skin tag. Similar changes at the proximal margin may result in a hypertrophied anal papilla. Chronic inflammation and fibrosis result in fibrotic lateral edges and exposed Internal anal sphincter (IAS) fibers at the base [9].

A chronic anal fissure is characterized by indurated edges caused by the exposure of anal sphincter fibers and formation of sentinel tags (pile) and hypertrophied papilla [10]. Lindsey et al suggested a standard definition for chronic anal fissures that the presence of a visible transverse internal anal sphincter fibers at the base of an anal fissure of duration not less than 6 weeks [11]. Severe painful anal ulceration after therapy with nicorandil has been observed for the past several years [12]. The size of anal ulcers which occur due to treatment with nicorandil varies and they have undermined edges like chronic anal fissure [13].

Chronic fissure patients will describe a deterioration cycle of recurrent pain, fear of defecation precipitating worsening constipation and even more severe pain. During the passage of stools, the local injury of the tear in the anoderm provokes a brief pain. After a free interval, the pain recurs with a dull character,due to the spastic and long lasting hypertonia of the anal sphincter. A vicious circle is created, since sphincter hypertonia provokes local ischaemia, with an increase of the pain and a new reflectory sphincter contraction. The pain and elevated sphincter pressure provoke retention of stools, sometimes with soiling. Stool retention in the anorectum makes the stool consistency firmer, with straining at defecation. This provokes new injuries of the anoderm, with further extension and chronicity of the fissure. Stimulation of the afferent fibres of the pudendal nerve can provoke dysuria and dyspareunia.

Several hypotheses concerning the pathophysiology of the chronic anal fissure were developed. It has been generally accepted that hypertonicity and hypertrophy of the internal anal sphincter is involved in the pathogenesis of anal fissure. Decades ago, fissures were considered to originate from chronic phlebitis in anal crypts [14] or from cryptitis with the formation of blind internal fistulas [15]. The dorsal location of most fissures was attributed to a lack of supportive tissue in a triangular zone dorsally in the anal sphincter, due to the elliptical arrangement of the sphincter fibres [16].

Mucosal ischaemia has also been hypothesized to result in the non-healing of anal fissure and progression of an acute anal fissure to a chronic fissure. Chowcat and co-workers [17] reported a decrease in resting anal pressure of 50% maintained for 4-6 years. Although evidence was mounting for a new hypothesis of hypertonicity driven ischemia, the link between manometry, ischemia, and healing had not been made until Shouten *et al* [18] assessed microvascular perfusion of the anoderm by laser doppler flowmetry and demonstrated significantly lower anodermal blood flow at the fissure site than at the posterior anal commissure of the controls. The second report by Schouten et al [19] in 1996 defined the ischemic hypothesis of chronic anal fissure by correlating the preoperative IAS hypertonicity, relative anoderm ischemia, and fissure non-healing with postoperatively normal IAS resting pressure, increased anoderm perfusion, healed fissures by 6 weeks. This newfound understanding not only explained the benefit of lateral internal sphincterotomy in permanently decreasing the resting tone of the IAS, but also opened up a number of new

avenues with which to medically treat chronic anal fissure. They also showed that IAS resting pressure was inversely related to the blood flow at the posterior midline and blood supply was significantly lower at the posterior midline than anywhere else in the anal canal in healthy individuals [17,18]. In patients with hypertrophied internal anal sphincter, this delicate blood supply is further compromised, thus rendering the posterior midline of the anal canal relatively ischemic.

Discussion

Anorectal manometry is the most well established and widely available tool for investigating anorectal function. A multitude of factors influence the measurement of the resting anal canal pressures. These include the technique used, the radial and longitudinal asymmetry along the anal canal, and variation in resting pressures and sphincter lengths among individuals of both sexes. Resting rectal pressure is approximately 10 mm Hg. Actually, changes in the intra rectal pressure are primarily a reflection of intra abdominal pressure changes, as the rectum itself has little peristaltic function.

In 1986, Gibbons and Read [19] reported that fissure patients had significantly elevated resting pressures which persisted over time. They were the first to suggest that chronically elevated IAS tone is the primary inciting event in the non-healing of acute fissures and further hypothesized that the hypertonic sphincter creates micro vascular hypertension and subsequently causes a relative ischemia to the lining of the anal canal.

A study performed by Thornton *et al* showed no correlation between fissure healing and incontinence and subsequent significant reduction in maximum anal resting pressure [20,21,22]. Moreover, another recent study made by Ho and Ho showed that anal fissure healing is not dependent on the level of the mean resting anal pressure [23]. Subsequent studies by Pascual *et al* found no statistically significant differences between healing and non-healing of chronic anal fissure after lateral internal sphincterotomy when compared with manometric and endosonographic findings [24].

Postmortem angiographic studies performed by Klosterhalfen *et al* [25] found that small perforating branches pierce the intermuscular septa perpendicular to the muscle. Lateral branches approaching perpendicularly toward an ellipse would be expected to have the weakest flow at the edges of the ellipse. There are no intramural collaterals between the branches of the inferior rectal artery in the anal canal wall and revealed an area of potential midline ischemia in the internal anal sphincter. Thus low perfusion can be attributed to the scarcity of small arteriolar anastomoses. Fissures generate in this region, when the resting sphincter pressure is sufficiently higher than the pressure in the small arterioles. Chronic anal fissures can therefore be considered as ischaemic ulcers.

Maria et al [21,26] demonstrated antiendothelial antibodies in patients with an anal fissure which damage the endothelial cells. Endothelial cell dysfunction is associated with reduced synthesis of nitric oxide, generating vasoconstriction and procoagulant activity. This mechanism also induces ischaemia of the anoderm and the formation of fissure.

Another theory is that internal anal sphincter is hypersensitive to beta-2 agonists and therefore the pathogenesis of anal fissure was sought in psychological stress. It also produces a sustained tonic raise in anal pressure [27,28]. Moreover, stress may cause molecular changes in beta-1 adrenergic receptors [29]. The postulated mechanism may precede development of anal fissure and may be also caused by anorectal infection. The first biochemical theory put forth by Minguez et al [30] suggests that, if the stretchiness of the anal sphincters is poor, eruption of tissues in the fissure region during every defecation causes the platelet products such as adenosine di-phosphate (ADP), adenosine tri-phosphate (ATP), 5-hydroxytryptamine (5-HT), platelet activation factor, as well as thrombin and substance P cause contraction of smooth muscles of internal anal sphincter and blood vessels, resulting in problems in the healing of anal fissure due to ischemia. When the endothelium is not traumatized, then these substances cause relaxation of normal blood vessels by releasing nitric oxide and prostacyclin I_2 (PGI_2) [31,32,33]. The end stage of the fissure as an ischemic ulcer is a fibrotic

lesion with a concomitant hypertrophic papilla and sentinel skin tag. Fibrosis is an important obstacle to healing and can result in an atonic ulcer. Chronic inflammation of the fissure can also provoke a local abscess and fistulisation.

Conclusion

Chronic anal fissures are ischemic ulcers, triggered and perpetuated by hypertonia of the anal sphincter. The dorsal location of most fissures can be attributed to local scarcity of arteriolar anastomoses and sphincter hypertonia. Chronicity of anal fissures results in fibrosis, end stage of repeated mechanical injuries and chronic inflammation. The concomitant hypertrophic papilla and skin tag are supplementary obstacles in the healing process. Therapeutic measures aiming at lowering the anal pressure and vasodilation are often successful [34]. Reducing trauma of defecation also plays an important role for anal fissure healing and recently doctors have created a new device – posterior perineal support. It brings a significant improvement in the symptoms of patients with anal fissure [35].

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