

Pharmacological Treatment of Anal Fissure – A Future Role in Primary Care

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INTRODUCTION

Anal fissure is a linear tear in the anal canal distal to the dentate line. It is a common condition affecting all age groups but is particularly common among young adults. The “gold-standard” for treatment of chronic anal fissure is lateral internal sphincterotomy. This surgical procedure results in a healing rate of up to 98% of patients⁽¹⁾. There has been greater understanding of the pathophysiology of anal fissure including the discovery of the roles of internal anal sphincter hypertonia⁽²⁾ and local ischaemia⁽³⁾. This has led to the use of various pharmacological agents which lower resting anal pressure and restore perfusion in the treatment of anal fissure. This “chemical sphincterotomy” which approximates the effect of its surgical counterpart is being investigated and used as possible first-line treatment for chronic anal fissure in many parts of the world. This mode of treatment offers a role in the primary care of anal fissure.

DIAGNOSIS OF ANAL FISSURE

The typical symptoms of anal fissure are anal pain during or after defaecation associated with the passage of bright red blood per rectum. The pain is often severe and may last for several minutes or hours after defaecation. The blood is usually separate from stool. This symptom sometimes results in the misdiagnosis of haemorrhoids. The latter condition is not usually associated with severe pain unless it is prolapsed and thrombosed. Altered blood or blood mixed with stool indicates the possible presence of other bowel pathology. Clinical examination will reveal the fissure to be a linear or pear shaped tear in the lining of the distal anal canal. There is often marked anal spasm which may preclude further digital or proctoscopic examination. An acute fissure is of short duration (less than a month) and has a fresh mucosal edge. With increasing duration, a chronic anal fissure results. This typically has indurated edges. The fissure base may reveal the presence of internal sphincter muscles fibres and a sentinel skin tag may be present.

TREATMENT

An acute anal fissure will usually heal spontaneously or with the use of simple measures. A high fibre diet with an adequate water intake is the cornerstone of treatment. Warm sitz baths may provide added symptomatic relief⁽⁴⁾.

Chronic anal fissure will not usually heal without some form of intervention. Treatment is directed at reduction of internal sphincter and anal canal pressure. Pharmacological means of inducing internal sphincter relaxation offer a new dimension of treatment in what was once an entirely surgical problem.

NITRATES

Nitric oxide is a neurotransmitter mediating the relaxation of the internal sphincter. This knowledge has led to the use of glyceryl trinitrate, which is a potent nitric oxide donor, for treatment of chronic anal fissure⁽⁵⁾. Topical GTN ointment or a GTN patch applied to the anal verge results in the healing of approximately two-thirds of chronic anal fissures^(6,7). A regimen using a “pea-sized amount” of 0.2% GTN ointment (approximately 0.5 g) applied twice a day to the anal canal for eight weeks is the most commonly prescribed form of treatment for chronic anal fissure. Alternatively, a 10 mg nitroglycerin patch applied close to the anal canal daily for eight weeks can be used. The majority of patients using GTN will develop headaches as a side effect of treatment. This is usually mild and transient. Occasionally headaches may be severe enough to warrant cessation of treatment⁽⁸⁾. This also implies that there is a possibility of fissure recurrence. A randomised controlled trial has reported the rate of recurrent symptoms to be 27% at two years⁽⁹⁾. A further course of GTN may be applied but lasting cures are better achieved with surgery when a fissure recurs.

CALCIUM CHANNEL BLOCKERS

Nifedipine and diltiazem act by blocking slow L-type calcium channels in smooth muscle causing relaxation. Studies show that both agents can decrease resting

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anal pressure in patients with chronic anal fissure^(10,11). Preliminary results of a multicentre study using local nifedipine showed that 95% of fissure healed with 21 days of therapy. However, the results are difficult to interpret as acute fissures were also included in the study. In another study using oral nifedipine for eight weeks⁽¹⁰⁾, healing was complete in nine out of 15 patients (60%) with chronic anal fissure and a further three were asymptomatic. Topical diltiazem has been reported to result in the healing of chronic anal fissure in between 60% to 75% of cases^(11,13). It has also been used to treat chronic anal fissures that have failed to heal with GTN⁽¹⁴⁾. Diltiazem cream also appears to cause less headaches than GTN ointment without a significant difference in healing rates between the two agents⁽¹⁵⁾.

OTHER SMOOTH MUSCLE RELAXANTS

α -adrenoreceptor antagonists⁽¹⁶⁾, B-adrenoreceptor agonists⁽¹⁷⁾ and parasympatho-mimetics such as bethanecol⁽¹³⁾ have been studied as alternative methods of "chemical sphincterotomy". Currently the experience with these agents is preliminary and well conducted clinical trials are awaited to test the efficacy of these agents.

BOTULINUM TOXIN A

Botulinum toxin A is a potent neurotoxin that binds to pre-synaptic cholinergic nerve terminals inhibiting the release of acetylcholine at the neuromuscular junction. When injected into the motor end-plate of a muscle, paralysis results that may last for three to four months.

Studies have shown that injection of botulinum toxin A into the anal sphincter lowers resting anal pressure and heals up to 82% of chronic anal fissure with a 6% recurrence rate at six months^(18,19). Transient faecal incontinence occurs in 7%⁽¹⁹⁾ of patients. A randomised trial comparing botulinum toxin with 0.2% GTN reported a healing rate of 96% and 60%⁽²⁰⁾. Various regimens have been used and there is controversy as to the optimal site of injection. The treatment is invasive and is associated with complications such as perianal thrombosis, sepsis and pain during injection. These problems minimise the widespread use of botulinum toxin despite evidence that support its effectiveness.

FUTURE DIRECTIONS

Pharmacological treatment of anal fissure offers an attractive alternative to lateral internal sphincterotomy. They are less invasive and the effects of treatment are reversible. The latter may be a desirable feature in eliminating the small risk of faecal incontinence that may be associated with surgery. Pharmacological

agents appear to heal approximately two-thirds of patients with chronic anal fissure and may be reasonably recommended as first-line treatment. Surgery can be used for failures of pharmacological treatment or fissures that recur frequently after cessation of local treatment. Currently in Singapore, most of the pharmacological agents reported on require special preparation within the context of a hospital pharmacy. A major step forward in adopting pharmacological agents as first-line treatment of anal fissure would be the availability of easy-to-use, appropriately formulated, proprietary topicals.

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