

Role of Glyceryl Trinitrate Topical Ointment in the Management of Chronic Anal Fissure

KHALID JAVEED KHAN, SHABBIR CHOCHAN, KHALID IRSHAD

ABSTRACT

Surgery has always been the treatment of choice for chronic anal fissure. However the results achieved with the use of topical ointments like glyceryl trinitrate have also been encouraging. A prospective study of 89 consecutive patients with chronic anal fissure treated with 0.2% topical glyceryl trinitrate ointment for a median duration of 9 weeks (range 2-16) weeks was performed.

Sixty three patients (71%) experienced healing of the fissure after using the topical application for a period of 2-5 weeks. Another 14 (15%) patients who did not respond to the therapy, got relieved after a duration of another 4-5 weeks. So overall 77(86%) patients got better with this therapy. Nine patients failed to follow up (10%). The remaining three patients requested for surgical option as they were reluctant to wait for the affects of the topical ointment. Headache and local irritation were the two main side effects reported by the patients.

Key words: Anal Fissure, diltiazem, nitroglycerine, calcium channel blockers, topical ointments.

INTRODUCTION

Anal fissure is a common anorectal problem, usually seen in people with sedentary lifestyle and constipation. The second major occurrence is seen in females in the later stages of pregnancy. It is associated with the spasm of the internal sphincter¹⁻³ except in postpartum patients⁴, and a reduction in mucosal blood flow⁵ with delayed or non healing of the ulcer. The aim of treatment is to improve the blood supply to the ischemic area to facilitate healing, if necessary by reducing resting anal pressure, a function of internal anal sphincter activity.

Traditional surgical techniques for treatment include anal dilatation or partial division of the internal sphincter. These procedures permanently lower the resting anal pressure and result in healing of the fissure in the majority of the patients, both of these methods may be complicated by permanent incontinence^{6,7}. This significant complication has led to a search for alternative therapies for the treatment of chronic anal fissure.

Chemical sphincterotomy has been tried using various agents including glyceryl trinitrate (GTN)⁸⁻¹⁰, calcium channel blockers such as nifedipine¹¹ or diltiazem¹²⁻¹⁴, and botulinum toxin¹⁵. This study was undertaken to evaluate the efficacy of topical GTN in the treatment of chronic anal fissure, to assess recurrence rates and to determine whether recurrent fissures would be amenable to further chemical sphincterotomy.

Department of Surgery, Fatima Jinnah Medical College/Sir Ganga Ram Hospital, Lahore
Correspondence to Dr Khalid Javeed Khan, Associate Professor Surgery

PATIENTS AND METHODS

Patients presenting during the outpatients clinics of one of the three surgical units at Sir Ganga Ram Hospital were included in the study. The duration spans from November 2006 to November 2009. All patients presenting to the outpatients were included in the study, the proformas were filled and treatment plans were explained to the patients. Those below 12 years of age and not willing to accept this treatment were excluded from the study. Patients with systemic disease like hepatitis or ESLD were also excluded. Chronic anal fissure was considered to be present if the patient presented with a history of painful defecation for at least six weeks duration which had failed to resolve with stool softeners and simple remedies. Examination typically revealed a fissure with fibres of the internal anal sphincter visible in the base, induration or sentinel pile. Age ranged from 19-64 years. Out of all the patients included in the study 56(63%) were females and 33(37%) were Males. Eight patients included in the study were recurrence after anal dilatation. 3 patients were recurrence after previous chemical sphincterotomy. Seventy one(80%) patients had posterior anal fissure. Nine(10%) had anterior fissure. Five(6%) had both anterior and posterior fissure. Three(4%) had multiple mucosal breaches through out the circumference.

Patients were advised to massage the affected area with 0.2% GTN cream for 3-5 minutes making sure that it is not applied in the anal mucosa. The procedure is to be repeated 2-3 times a day depending on complaints of headache. Patients were advised high fibre diet and ispaghula husk to overcome the bowel irregularities.

RESULTS

Sixty three patients (71%) experienced healing of the fissure after using the topical application for a period of 2-5 weeks. Another 14 (15%) patients who did not respond to the therapy, got relieved after a duration of another 4-5 weeks. So overall 77(86%) patients got better with this therapy. Nine patients failed to follow up (10%). The remaining three patients requested for surgical option as they were reluctant to wait for the affects of the topical ointment. Headache and local irritation were the two main side effects reported by the patients.

A median follow up of 32(range 14-67) weeks is available for 80(90%) is available who were managed successfully with GTN. 31(35%) of the treated patients developed mild to moderate symptoms during the follow up period but they all were managed with reassurances and remedies like stool softeners and high roughage diet.

DISCUSSION

Chronic anal fissure may be treated by chemical or surgical sphincterotomy. Left lateral internal sphincterotomy results in healing for up to 95% of patients but there remains a significant risk of incontinence^{6,7}.

GTN remains the standard for chemical sphincterotomy against which other newer treatments have to be compared. Within controlled clinical trials, healing with GTN for chronic anal fissure has been achieved in 45-87% of the patients^{6,8,9,16,17}. However significant side effects such as headache, tachyphylaxis and occasional loss of flatus control have been reported^{6,8,9,16,17}. A study conducted previously reported ineffectiveness of the GTN as treatment of choice by reporting poor long term outcome, with only 6% of patients healed at 12 months¹⁸.

Research for any affective chemical agent for sphincterotomy has to answer two questions, namely does it work and for how long does it last? Oral calcium such as nifedipine and diltiazem have been shown to reduce mean resting anal pressure by between 21 and 28 percent of healthy volunteers^{11,12}. Additionally healing of fissure has been reported with the use of oral nifedipine^{R11} and diltiazem¹². Although changes in diastolic blood pressure are negligible when using oral calcium channel blockers, postural dizziness can occur. The principal side effects of oral nifedipine and diltiazem are facial flushing and headache^{12,13}.

Topical diltiazem is associated with fewer side effects, perhaps less systemic absorption compared to GTN. Previously the affect of GTN on the mean

resting anal pressure of between 22 and 28 percent in healthy volunteers and in patients with chronic fissure has been demonstrated¹²⁻¹⁴. Dose response studies have reported that the concentration of 2% due to its less absorbability and only 0.2% for GTN is safely recommended with equal efficacy and acceptable side effects¹².

A healing rate of 86% with in the follow up periods is quite effective and comparable to other topical agents. A similar study showed a 67% success rates with diltiazem topical application^{R19}, however that study shows the efficacy of diltiazem with lesser side effects compared to GTN.

In conclusion, topical 0.2% GTN appears to be a well tolerated method of chemical sphincterotomy for chronic anal fissure. Prospective randomized trials are required to evaluate the efficacy of different topical agents. Long term follow up is also needed to assess the risk of recurrent fissure after initial healing with topical agents

REFERENCES

1. Kuijpers H C. Is there really sphincter spasm in anal fissure? *Dis Colon rectum* 1983; 26: 493-4.
2. Gibbons C P, Read N W. Anal hypertonia in fissures; cause or effect? *Br J Surg* 1986; 73: 443-5.
3. Farouk R, Buthie GS, Macgregor AB, Vartolo DCC. Sustained internal anal sphincter hypertonia in patients with chronic anal fissure. *Dis of colon and rectum* 1994; 37: 424-9.
4. Corby H, Donnelly VS, O'Herlihy C, O'Connell PR. Anal canal pressures are low in women with postpartum anal fissure. *Br J Surg* 2007; 84: 86-88
5. Klosterhalfen B, Vogel P, Rixen H, Mittermayer C. Topography of the inferior rectal artery: a possible cause of chronic, primary anal fissure. *Dis colon Rectum* 1999; 32: 43-52
6. Pitt J, Boulos PB. Chemical sphincterotomy for anal fissure. *Colorectal diseases* 1999; 1: 2-8
7. Khubchandani IT, Reed JF. Sequelae of internal sphincterotomy for chronic anal fissure. *Br J surg* 1989; 76: 431-4
8. Lund JN, Scholefield JH. A randomized, prospective, double blind, placebo controlled trial of glyceryl trinitrate ointment in the treatment of chronic anal fissure. *Lancet* 1997; 349: 11-14.
9. Carapeti EA, Kamm MA, McDonald PJ, Chadwick SJ, Melville D, Phillips RKS. Randomised controlled trial shows that glyceryl trinitrate heals anal fissure, higher doses are not more effective, and there is a high recurrence rate. *Gut* 1999; 44: 727-30.
10. Farouk R, Gunn J, Duthie GS. Changing patterns for treatment of chronic anal fissure. *Ann R Coll Surg Engl* 1998; 80: 194-6.
11. Antropoli C, Perotti P, Rubino M, Martino A, De Stefano G, Migliore G et al. Nifedipine for local use in chronic anal fissure: Preliminary results of a multicentre study. *Dis Colon Rectum* 1999; 45: 19-22.

12. Carapetti EA, Kamm MA, Evans BK, Phillips RKS. Topical diltiazem and bethanecol decreases anal sphincter pressure without side effects. *Gut* 1999; 45: 719-22.
13. Carapetti EA, Kamm MA, Phillips RKS. Topical diltiazem and bethanecol decrease anal sphincter pressure and heal anal fissure without side effects. *Dis Colon Rectum* 2000; 43: 1359-62
14. Bhardwaj R, Vaizey C, Boulos P. Topical 2% diltiazem in the treatment of chronic anal fissure. *Colorectal diseases* 2000; 2(suppl 1): 16(abstract).
15. Brisinda G, Maria G, Bentivoglio AR, Cassetta G, Gui D, Albanese A. A comparison of injection of botulinum toxin and topical glyceryl trinitrate ointment for the treatment of chronic anal fissure. *N Engl J med* 1999; 341: 65-9.
16. Altomare DF, Rinaldi M, Milito G, Arcane F, Spinelli F, Nardelli N et al. Glyceryl trinitrate for chronic anal fissure healing or headache? Results of a multicentre, randomized, placebo-controlled double blind trial. *Dis Colon Rectum* 2005; 43: 174-9.
17. Richard CS, Gregoire R, Plewes EA, Silverman R, Burul C, Buei D et al. Internal sphincterotomy is superior to topical nitroglycerine in the treatment of chronic anal fissure: results of a randomised, controlled trial by the Canadian Colorectal Surgical Trials Group. *Dis Colon Rectum* 2000; 43: 1048-57.
18. Hyman NH, Cataldo PA. Nitroglycerine ointment for anal fissure; effective treatment or just a headache? *Dis Colon Rectum* 1999; 42: 383-5
19. Knight JS, Birks M, Farouk R. Topical diltiazem ointment in the treatment of chronic anal fissure. *Br J Surg* 2001; 88: 553-556.