ORIGINAL ARTICLE

Glyceral Trinitrate is an effective Primary Treatment in Chronic Anal fissure

ARUJ ALAM, MUHAMMAD SHOAIB, SOHAIL ANJUM, AFTAB AHMAD

ABSTRACT

Background: Chronic Anal Fissure (CAF) is a common painful perianal condition and well-known painful entity. Non-surgical treatment with 0.2% Glyceryl Trinitrate (GTN) has shown to be an effective in relieving symptoms and ultimately helpful in healing process.

Aim: To analyze the effectiveness of 0.2% Glyceryl Trinitrate paste in the treatment of ch anal fissure. **Study Design**: Descriptive analytical type of study.

Place and duration of study: This study was conducted at Chaudhary Rehmat Teaching Hospital affiliated with Continental Medial College Lahore from July 2013 to Dec 2014.

Methodology: Ninety two patients were included who had agreed for non-surgical treatment with 0.2% Glyceryl Trinitrate paste. Patients were prescribed administration of 0.2% GTN paste with device 1.5 cm to 2 cm inside the anal canal twice daily for 3 months. Data was collected on a proforma included detailed history with identifying etiological factors, defecatory pain analysis with VAS and serial perrectal examination finding on F/U visits. All the patients were instructed to keep follow up in OPD at 2,4,6,8,10 and 12 weeks and thereafter evaluated for relief of symptoms.

Result: Out of these 92 patients 78(84%) were females with mean age 36.9±7.8 years. More than 50% of patients were pain free at 6 weeks period of continuous use of local application of 0.2% GTN paste and 85% patientshad complete resolution of defecatory pain by 12 weeks and 77% of patients were found to have healed up fissure at 12 weeks. Sixteen patients complained of headaches in the initial weeks of local application of GTN paste which caused 5 of them to lost F/U later.

Conclusion: Primary management with 0.2%GTN paste is a cost effective method of treatment with better compliance in our community mostly of low economic levels.

Keywords: Chronic anal fissure, Glyceral Trinitrate, perianal pain, Rectal bleeds

INTRODUCTION

Anal fissure is a breech in the mucocutanoeus junction at anal canal mostly at posterior angle. Patients usually presentwith severe anal pain mostly during defecation and often rectal bleeding. Both sexes are equally affected with more patients from younger age groups. Acute anal fissures can heal spontaneously or with simple symptomatic treatment and dietary changes. A large proportion of patients' progress to develop chronic anal fissure. An anal fissure is considered chronic after symptoms persist for more than 6 weeks. It is described as a linearulcer with exposed fibres of internal anal sphincter in some instances. Anal skin tags or sentinel pile is another association commonly seen in chronic anal fissures. Most of the anal fissures are idiopathic without any chronicunderlying disease. Chronic constipation, altered bowel habits and low dietry fibre intake are commonly found in our public. Posterior anal fissures are common due to anatomical considerations i.e., lack of tissue strength at posterior

Department of Surgery, Lahore Medical & Dental College/ Ghurki Trust Teaching Hospital, Lahore

Correspondence to Dr.Aruj Alam, Assistant Professor Surgery, Continental Medical College, Lahore Email: arujgardezi@hotmail.com

wall. Pregnancy is another common condition associated with mostly anteriorly placed anal fissures. Secondary anal fissures are seen associated with causes like crohn's disease, syphilis, human immunodeficiency virus (HIV) or tuberculosis. and are most appropriately treated by addressing the underlying disease process¹.

Gold standard treatment of chronic anal fissure is lateral anal sphincterotomy, having superior healing rates. Standard surgical treatment does not usually require long hospital stay and occasionally have led to some worrying complications like incontinence. Though it's not very expensive, still patient in our community are apprehensive about cost and long stay away from home and work. Cultural issues are hindrance in early consultation in these symptoms, also increase chronicity of the problem. In such circumstances, non-surgical treatment for this ailment is much needed2. Alocal application of Glyceryl Trinitrate has been shown to be an effective treatment for chronic anal fissure. It decreases anal tone and ultimately heals the anal fissure³. Local Application of GTN is associated with a significant reduction in resting anal pressure and a reduction in pain scores⁵. Long-term healing can be achieved in 59% of patients treated in this way⁶. Headache as a complication of local perianal application of GTN paste is not infrequent. Significant side-effects of headache and poor fissure healing rates have discouraged some from using a chemical sphincterotomy as a treatment option for chronic anal fissure⁶. Anal advancement flaps and botulinum toxin (Botox) injection combined with a fissurectomy represent alternative surgical approaches that preserve anal sphincter integrity¹⁰.

MATERIAL AND METHODS

This descriptive analytical study was carried out in OPD of Chaudhary Rehmat Hospital township Lahore during the study period from July 2013 to Dec 2014. Data was collected from 92 patients which were seen and followed up in Data was collected on a proforma and was analyzed. Following were inclusion and exclusion criteria for patient data collection.

Inclusion Criteria

- 1. All patients with signs and symptoms of anal fissure for more than 3 months
- 2. Chronic anal fissure with its associated features like sentinel pile, hypertrophied papillae etc
- 3. Patient with recurrence after surgical and medical therapy as well

Exclusion criteria

- Age less than 18 years with H/O IHD and medications including nitrates
- 2. Anal fissure presented in pregnancy
- 3. Anal fissure associated with inflammatory bowel disease like crohn's disease and tuberculosis
- 4. Immunocompromised patient

Data of all included patient seen in OPD were collected on prescribed form. Baseline assessment included duration of symptoms pain at defecation was evaluated on a VAS (visual analoguescore). Per rectal examination findings were noted as skin tag (sentinel pile), anal fissure and exposed sphincter were noted. Follow up visit were scheduled at 2, 4, 6,8,10 and 12 weeks duration after starting treatment with 0.2% GTN paste. Follow up visits included assessment of symptoms, examination, compliance to instructions and pain assessment at defecation by VAS. During initial follow up visits, symptomatic treatment like routine analgesia if necessary and ispaghullah husk were advised for severe pain and constipation respectively. Resolution of defecatory pain and fissure healing were categorical variables. Each of the outcome was analyzed by data collected during follow up visits and at the end of treatment.

RESULTS

Between July 2013 and Dec 2014 ninety two patients were enrolled in the study as per fixed criteria after

informed consent for non-surgical treatment. Most of the patient were female as M:F ratio 14:78. The mean age of patients was 37 years (range 21-56 years), the mean length of duration of symptoms and sign at presentation was 6 months (range 3-9 months). Perianal pain and constipation were the commonest symptoms at presentation found in all patients. Bleeding PR was found in 53 patients (57%) at presentation Figure 1. More than 50% of patients were pain free at 6 weeks follows up. 78(85%) patients showed almost complete resolution of defecatory pain at 12 weeks treatment with GTN 0.2% paste Fig 2. Twenty patients (21%) found to have healing fissure at 6 weeks of treatment and 71 patients (77%) had complete healing after 12 weeks. Treatment with 0.2% GTN paste was found unsuccessful in 9patients only at 12 weeks. Twelve patient experienced headache at commencing treatment but they continued treatment after satisfactory management for headache. Five patients lost to FU after 4-6 weeks of treatment duration.

Fig. 1: Symptoms at presentation

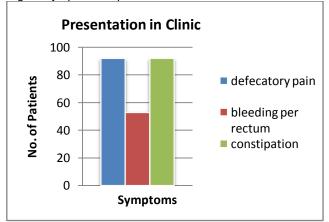
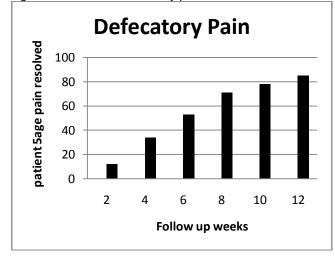
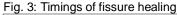
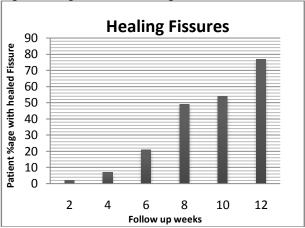


Fig. 2: Resolution of defecatory pain







DISCUSSION

Local 0.2% GTN paste application is an effective alternate to surgical treatment. In our study, 85% of patients had complete resolution of defecatory pain and 77% of patients showed healing fissures in 12 weeks treatment with local application of 0.2% GTN paste. It is comparable to the study by Latif A etal¹³ in 2013 which had 74 % success rate with 0.25 GTN. In a study y EL Tinay OE et al14 complete symptomatic relief was achieved in all patients with one month therapy with 0.2% GTN ointment. In a study conducted by Siddique MI et al¹⁵ in Bangladesh, after 8 weeks of complete treatment 80.64% patients in GTN ointment group were pain free with healed fissure 67.74% patients in contrast to surgical sphincterotomy showing 100%. In a study, Punche JJ et all¹⁶ showed initially significant difference in improvement rate of 45% with standard measure, 62.5%with NTG and 80% DTZ p<0.01but cure rates 27% ST, 40%NTG and 39% DTZ. Topical 0.2% GTN is an effective first line agent in managingchronic anal fissure. The associated side effects and recurrence remains a matter of concern 76% showed healing of fissure and relief in symptoms¹⁷. Fissure healing was 100% in surgical group as compared to 74% in medical treatment group. Complications were recorded and were found to be headache with medical treatment while the most feared complication with surgery i.e., incontinence was not found 13

The use of nitrates has been shown to reduce anal hypertonia and many clinical contexts it has become the first line therapy for chronic anal fissure. The topically applied nitroglycerine has had shown good therapeutic role in treatment of anal fissures and identified in reduction of the number of surgical procedures, especially in several European countries. Several initial trials that were conducted revealed a reversable relaxation 20-23 but without

standardization of the dose. A study focusing on the optimal nitroglycerine ointment dose and dosing interval was carried out by bailey and colleagues²⁴. Glyceryl trinitrate has been tested mainly in two formulation 0.2-0.4%. Randomized controlled trials conducted with 0.2% GTN ointment had cure rates of between 50-68%^{25,26}. A recent cochrane review of the medical therapy for anal fissure demonstrates that as regards the cure rate topical nitrates are marginally but significantly superior to placebo. It is important to note the significant effect these drugs had on reducing pain²²⁻²⁴ and positive effect on the patient's activity and vitality, wellbeing. physical fundamental components of quality of life. 27 In our experience, treatment with topical GTN for less than eight weeks duration is likely to be unsuccessful in cases of true chronic anal fissures; indeed some fissures may heal partially within eight weeks but will fully heal completely if treated with GTN paste for more longer duration²⁸.

The most common adverse event correlated with topial therapy of GTN is headache reported in an average of 25% of the patients and is manageable with mild analgesics. ²⁹Although frequentdevelopment of headache doesnot seems to result in reduced compliance. In fact , clinical experiences has provedthatperianal pain associated with anal fissures is definitely more worrying than the headache and thereforeinterruption of therapy due to this adverse event is rare. ^{26,27}

Topical glyceryltrinitrate is economical and has a satisfactory healing rate without reported fecal incontinence. Its effectiveness however depends on patient's compliance which may be poor in view of some headache. It is proved as first line of treatment for chronic anal fissure but surgery has superior results in terms of faster healing.

CONCLUSION

Glyceryl Trinitrate is a cost effective first line treatment strategy for the management of chronic anal fissure. Lateral sphincterotomy remains effective but should be reserved for the patients who fail to respond to initial chemical sphincterotomy or GTN therapy. GTN therapy is good alternative mode of therapy for patients who refuse surgery and prefer medical line of treatment.

REFERENCES

- R Bhardwaj, MC Parker, Modern Perspectives in Treatment of Chronic anal Fissure, Ann R CollSurgEngl2007; 89: 472–478
- Utizg MJ, Kroesen AJ, Buhr HJ. Concepts in pathogenesis and treatment of chronic anal fissure a

- review of the literature. Am J Gastroenterol. 2003; 98(5): 968.
- Miguel M, Belen H, Adolfo B. Chronic anal fissure. Curr Treatm Opt Gastroenterol. 2003;6:257–262.
- Loder PB, Kamm MA, Nicholls RJ, Phillips RK. 'Reversible chemical sphincterotomy' by local application of glyceryl trinitrate. Br J Surg 1994; 81: 1386-9.
- Kennedy ML, Sowter S, Nguyen H, Lubowski DZ. Glyceryl trinitrate ointment for the treatment of chronic anal fissure: results of a placebo-controlled trial and long-term follow-up. Dis Colon Rectum 1999;42:1000-6
- Altomare DF, Rinaldi M, Milito G, Arcana F, Spinelli F, Nardelli N, et al. Glyceryl trinitrate for chronic anal fissure--healing or headache? Results of a multicenter, randomized, placebo-controled, double-blind trial. Dis Colon Rectum 2000;43:174-9.
- Libertiny G, Knight JS, Farouk R. Randomised trial of topical 0.2% glyceryltrinitrate and lateral internal sphincterotomy for the treatment of patients with chronic anal fissure: long-term follow-up. Eur J Surg 2002;168:418-21.
- 8. Nelson RL. Operative procedures for fissure in ano. Cochrane Database Syst Rev 2010;(1):CD002199.
- Nyam DC, Wilson RG, Stewart KJ, Farouk R, Bartolo DC. Island advancement flaps in the management of anal fissures. Br J Surg 1995;82:326-8.
- Scholz T, Hetzer FH, Dindo D, Demartines N, Clavien PA, Hahn loser D. Long-term follow-up after combined fissurectomy and Botox injection for chronic anal fissures. Int J Colorectal Dis 2007;22:1077-81.
- Knight JS, Birks M, Farouk R. Topical diltiazem ointment in the treatment of chronic anal fissure. Br J Surg 2001;88:553-556.
- 12. Samim M, Twigt B, Stoker L, Pronk A. Topical diltiazem cream versus botulinum toxin a for the treatment of chronic anal fissure: a double-blind randomized clinical trial. Ann Surg 2012;255:18-22.
- Latif A, Ansar A, Butt MQ. Morbidity associated with treatment of chronic anal fissure. Pak J Med Sci 2013;29(5):1230-1235.
- El Tinay OE, Guraya SY. The use of 0.2% Glycerol Trinitrate ointment for an anal fissure. Saudi J Gasteroenterol. 2005;11:40-44.
- Siddique MI, Murshad KM, Majid MA. Comparative study of lateral sphincterotomy versus local 0.2% glycera trinitrate ointment for the treatment of chronic

- anal fissure. Bangaladesh Res Counc Bull. 2008;34:12-15.
- Puche JJ, Garcia-Coret MJ. Villalba FL, Ali Mahmoud I, Roig JV. Local Treatment of a chronic anal fissure with diltizem vs. nitroglycerine-A comparative study. Cir Esp.2010;Apr, 87(4):224-30.
- Hashmi F, Memon NM, Khan AM. Efficacy and side effects of glyceryltrinitrate in management of chronic anal fissure. J Ayub Med coll Abbottabad. 2012 Jan-Mar; 24(1):21-22.
- 18. Collin EE, Lund NJ. A review of hroni anal fissure management. Tech Coloproctol 2007; 11:209-223
- Lund JN, Nystrom PO, Coremans G et al .An Evidence based treatment algorithm for anal fissure. Tech Coloproctol 2006; 10:177-180.
- Gorfine SR (1995) Topical nitroglycerine therapy for anal fissures and ulcers. N England J Med 333:1156-1157
- Lund JN, Armitage NC, Scholefield JH (1996) Use of glyceryltrinitrate ointment in the treatment of anal fissure. Br J Surg 83:776-777
- Kennedy ML, Sowter S, Nguyen H, Luowski DZ. (1999) Glyceryltrinitrate ointment for the treatment of hroni anal fissure: results of a plebocontrolled trial and longterm follow up. Dis Colon Retum 42:1000-1006
- Loder PB, Kamm MA, Nicholls RJ et al. (1994). Reversable chemical sphinterotomy by local application of glycerol trinitrate. Br J Surg 81:1386-1389.
- 24. Bailey HR, Beck DE, Billingham RP et I(2002). A study to determine the nitroglycerine ointment dose interval the best promote the healing of chronic anal fissures. Dis Colon Rectum 45: 1192-1199.
- Lund JN, Scholefield JH(1997) A Randomized prospective double blind placebo-controlled trial of glyceryl trinitrate ointment in treatment of anal fissure. Lancet 349:11-14
- 26. Nelson R (2004) A systematic review of medical therapy for anal fissure. Dis Colon Rectum 47:422-431
- Griffin N, Acheson AG, Tung P, Sherad C, Glzerook C, Scholefield JH (2004). Quality of life in patients with chronic anal fissure. Coloprocto 5:143-147I
- 28. Lund JN, Scholefield JH. Follow-up of patients with chronic anal fissure treated with topical glyceryl trinitrate. Lancet 1998;352:1681
- Nelson R (2006) Nonsurgical therapy for anal fissure.
 Cochrane database system Rev 18: CD003431.