



Comparative Study of Glyceryl Trinitrate Ointment Versus Lateral Internal Sphincterotomy in Management of Chronic Anal Fissure

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Abstract

Background: Anal fissure is a common benign condition. An anorectal problem is defined as a split in the anal canal mucosa that extends from the dentate line to the anal verge. Chronic anal fissure is defined by a history of symptoms present for more than 6-8 weeks' duration and with a triad of external skin tags, an ulcer with rolled edges, and a base exposing the internal sphincter.

Objectives: The objective of this study is to compare the difference in outcome and the effectiveness between open partial lateral anal sphincterotomy and application of topical 0.2% nitroglycerin ointment for the treatment of chronic anal fissure.

Methods: This was a clinical prospective randomized controlled study. A hundred thirty consecutive cases with a clinical diagnosis of chronic anal fissure were recruited in the study. All recruited patients met the study inclusion criteria and were randomly assigned to one of the two groups. Group A was managed conservatively using topical 0.2% nitroglycerin ointment, whereas Group B underwent open partial lateral anal sphincterotomy. Both groups were followed up at 1 week, 2 weeks, 4 weeks, and 6 weeks after the treatment.

Results: All the patients complained of pain. A total of 104 (80%) patients had pain with constipation, whereas 65 (50%) patients had bleeding per rectum. Upon clinically examining the anal area, tenderness was elicited in all 125 (96%) patients. Group A included 65 (30 females and 35 males) cases treated with topical 0.2% nitroglycerin ointment and Group B included 65 (25 females and 40 males) cases who underwent open partial lateral anal sphincterotomy. In Group A, only 40 patients with fissures were successfully treated (62%). By contrast, 62(95.5%) patients with fissures in Group B were successfully treated, and only three (4.5%) remained uncured. Two of the three patients suffered from post-operative perianal abscess and the remaining patient is suffered from transient flatus incontinence which persist for 8 weeks.

Conclusion: This study demonstrates that open partial lateral internal sphincterotomy is superior to topical 0.2% nitroglycerin application in the treatment of chronic anal fissure, with good symptomatic relief, high rate of

healing, fewer side effects, but because topical GTN is safe and well tolerated the surgeon can start with it according to the patient status.

Keywords: Chronic anal fissure; Open partial lateral anal sphincterotomy; Topical 0.2% nitroglycerin

Introduction

Anal fissure is one of the most common lesions to be considered in the differential diagnosis of anal pain. It typically causes episodic pain that occurs during defecation and persists for 1–2 hours afterward [1] anal fissure is one of the most painful condition encountered in surgical practice and cause considerable morbidity and reduction in quality of life. The most consistent finding in typical fissures is spasm of the internal anal sphincter, which is so severe that the pain caused by the fissure is thought to be due to ischemia of the sphincter [2]. Morbidity from operative procedures, mainly incontinence, was once thought to be extremely rare [3], but has been substantial in some recent reports [4]. The choice of treatment remains difficult for the following reasons. Although surgery is highly efficacious and successful in treating the fissure in more than 90% of patients, in a systematic review of randomized surgical trials, the overall risk of incontinence was approximately 10% [5]. This was mostly due to flatus incontinence, and there are no reports delineating the duration of this problem. Regarding medical treatment, in a similar systematic review combining all analyses in which a placebo was used as the comparison group [6], the healing rate in the placebo group was found to be 35%. This was a level of response that was fairly uniform across studies (standard deviation: 12%). The medications being tested in the meta-analysis (nitroglycerin ointment, botulinum toxin injection, and calcium channel blockers) must have their efficacy viewed in the context of this placebo effect and also in the context of a cure rate for surgery that often exceeds 95% [5]. In the combined analyses, nitroglycerin ointment was found to have a healing rate of about 55%. In addition, with nitroglycerin ointment, the most investigated medical treatment, headache was common, occurring in almost 40% of patients in the combined analyses and often severe enough to stop treatment [6]. Therefore, it would be advantageous if the risk of incontinence could be reduced after the surgery or if the success rate of various other medical treatments is increased to that reported after a surgery, but with less risk of headache. The risk of using such treatments is not high, as patients mainly only experience headache while using the nitroglycerin ointment, without any apparent adverse effect in the long term. Medical treatments can therefore be used in individuals wanting to avoid surgical treatment, and surgery can be reserved for treatment failures in adults with chronic typical fissure. We wanted to study scientifically whether the outcome of surgical management among these patients is better than conservative (medical) approach.

Patients and Methods

This was a clinical prospective randomized controlled study done in cooperation with clinical pharmacology department in Benghazi university and surgical department of aljalla university hospital benghazi including 130 patients presented with chronic anal fissure divided into two groups. Group A include 65 patients with chronic anal fissure treated with local glyceryl trinitrate ointment 0.2% (liposomal base) applied twice daily for 6 weeks. Group B include 65 patients managed by lateral internal sphincterotomy, all patients treated by same surgeon using same method and surgical technique of sphincterotomy.

Inclusion criteria and exclusion criteria

- patient willing to enrolled in this study
- all cases of anal fissure of more than 6 weeks' duration.
- anal fissure with associated features of chronicity like sentinel pile or hypertrophied papillae

Patients on medication containing nitrate compound for medical condition, like ischemic heart disease, pregnancy, anal fissure with inflammatory bowel disease, immuno-compromized state or tuberculosis were excluded. The intensity of pain during defecation was assessed by using Visual Analogue Scale (VAS) this visual analogue was a 10 cm line on which 0 represent no pain and 10 the most severe pain.

Data collection procedure

130 consecutive cases of anal fissure diagnosed clinically with digital examination were registered to participate in the study. A written informed consent was obtained from all the patients after they were briefed about the procedures of fissure management. All patients met the inclusion criteria and were randomly assigned to one of the two groups. The demographic data including name, age, gender, and address were recorded. A topical anesthetic ointment (lignocaine gel) was routinely applied 5–10 minutes prior to the patients undergoing digital examination. The patients who were managed conservatively (Group A) were supplied with 0.2% nitroglycerin ointment, and were advised to rub the paste every 12 hours with a gloved finger. The treatment was carried out for 6 weeks. Patients were followed up at 1 week, 2 weeks, 4 weeks, and 6 weeks after the treatment with special consideration to pain relief, healing of fissure, and side effects of treatment. The pain severity was recorded with VAS method. Analgesics, sitz bath, and laxatives were standard options to treat pain. The patient is considered to be successfully healed when the breach in mucosa was completely treated and the patient had not experienced pain during defecation. Group B underwent open partial lateral anal sphincterotomy and the patients were followed up at 1 week, 2 weeks, 4 weeks, and 6 weeks after the treatment.

Data analysis

At the end of the study the data was collected and analysed statistically the qualitative data presented in the form of numbered percentage. Chi-square test was used as a test of significance for qualitative data in term of pain reduction and time taken for healing student t- test was used as a test of significance for quantitative data a p value of > 0.05 was considered significance.

Results

A total of 130 patients with clinical diagnosis of chronic anal fissure were included in this study. In Group A, the minimum age of the participants was 20 years and the maximum age was 58 years (mean age: 39 ± 11.3 years). In Group B, the minimum age of the participants was 21 years and the maximum age of the participants was 55 years (mean age: 37.4 ± 12.03 years). A total of 55 (42.7%) participants were female and 75 (57.3%) were male. All the 130 patients complained of pain (100%). However, the severity of pain varied. The mean duration of symptoms in group A was 17.2 ± 11.2 weeks where as in group B was 16.8 ± 11.9 weeks. Both groups were comparable regarding mean pain score during defecation before treatment-group A 8.6 ± 0.9 vs. 8.5 ± 1.2 in group B ($p < 0.5$). Bleeding during defecation was present in 75% of group A and 80% of group B patient whereas constipation was present in 39 patients 60% in group A and 45 patients in group B 69.8%. All patient in both groups had posterior fissure.in group A 30 patient had anal tag where as in group B 38 patients had skin tag.

Pain score after treatment

In group A (GTN OINTMENT) mean pain score at first follow up was 8.3+ 1.3 on VAS on subsequent follow ups at the end of 1st week, 3rd and 6th week the mean pain score was 7.5+1.5, 3.00+2.1, 2.64+2.1 respectively. For group B (lateral internal sphincterotomy) the mean pain score at first follow up at (72hr) was 3.2+1.06. on subsequent follow ups at the end of 1st, 3rd and 6th week mean pain score was 1.4+1.2, 0.52+0.9, 0.24+0.8 respectively although patients in both groups had perceptible pain relief as compared to pretreatment levels at 6 weeks of therapy but the decrease in mean pain score in group B (surgically treated) as compared to group A (GTN group) at the end of 6th weeks was statistically significant ($p < 0.5$). However complete relief of pain was observed in 39 out of 65 patients after treatment with 0.2% GTN ointment whereas 62 out of 65 patients had complete relief of pain after surgical management at the end of 6th week the remaining 3 in group B had complication required more time to heal two had post-operative abscess and the other one had transient flatus incontinence. Therefore, number of patients who had complete relief of pain after surgical treatment was statistically significant as compared to patients who were medically treated with 0.2% GTN ointment. None of the patient in either group had complete healing at the end of 1st week, however at the end of 3rd week 20 patient in group A and 60 patients in group B had complete healing of fissures complete healing was observed in 38 out of 65 in group A (GTN GROUP) whereas 63 out of 65 in group B (lateral internal sphincterotomy) had completely healed fissures at the end of six weeks ($p < 0.5$).

Side effect complication of the treatment

Except headache which was reported in 26 (40%) patients in group A no other side effect was seen in this group. None of the patient in group A had to stop medication due to side effects, whereas only two patients out of 65 in group B had small perianal abscess which treated with small incision, and one out of 65 had flatus incontinence which is relieved after 6 weeks from the procedure.

Recurrence

Only 38 patients in group A had healed fissure at the end of 6th week, so recurrence was observed in these patients only 5 of these 38 patients (14.75%) had recurrence of the fissure at same site at 3rd month follow up 63 patients in group B had healed fissure at the end of 6th weeks no recurrence was noted at 3rd month follow up [Table 1](#).

Table 1: Results after 6 weeks of treatment.

	0.2% nitroglycerin (n = 65)	Open lateral internal sphincterotomy (n = 65)	<i>p</i>
No pain after the treatment	39	62	0.0001
No bleeding after the treatment	17	65	0.001

No headache with the treatment	39	65	0.0001
No incontinence after the treatment	65	64	>0.5
Fissures healed after 6 weeks	38	63	0.0001

Discussion

Historically, the most common approach for relieving the pain associated with spasm of chronic adult anal fissure is surgical, yet no placebo-controlled surgical trials have been carried out. Surgery is usually associated with high costs, increased recovery time, and risk of incontinence. Therefore, by the late 1990s when alternatives to surgery were sought rather than turning back to older treatments, such as lubricants and numbing agents, newer medications were investigated—in each case, a medication that was known to relax muscle spasm was used. Such medications included nitroglycerin ointment, injection of botulinum toxin, and calcium channel blockers, which are either given as tablets or applied topically. The encouraging results of early clinical trials of 0.2% nitroglycerin suggested that it might find a role in the treatment of anal fissures. Most studies tried to establish the role of 0.2% nitroglycerin as an exogenous nitric oxide providing agent, which is an important neurotransmitter mediating internal anal sphincter relaxant. In these previous studies, anal manometry and assessment of squeeze pressure were the methods used to evaluate the effectiveness of 0.2% nitroglycerin. Manometry showed 2% reduction in maximum resting pressure and squeeze pressure fell by 11%. This is parallel to criteria used in this study, wherein place of objective evidence and improvement in pain and healing of fissure were used to assess treatment efficacy. Gorfine [7] adopted a similar methodology in 1995 that used clinical evidence to assess the efficiency of treatment. A visual analog scale for pain adopted from a previous study proved to be effective yet simple to evaluate the subjective improvement [8]. It was seen that the pain score fell more progressively and permanently from 10 to less than 1 with surgery as compared with 10 to 3 for topical ointment, but after 6 weeks, the score again rose to 6 or 7 in patients treated with topical ointment. Prior to widely adopting this form of treatment, a comparison with the current standard open lateral internal sphincterotomy must be made. In this study, using a 0.5 mL dose of 0.2% nitroglycerin, we have observed healing of the fissure in 62% of patients after 6 weeks, which is comparable with the results of Lund and Scholefield [9] and other studies [2,7,10]. Although 0.2% nitroglycerin was less effective in healing the fissures, it was quite effective in reducing the symptoms and minimizing the pain when used. Once 0.2% nitroglycerin was discontinued, pain recurred in a few patients, following which almost 40% of patients required surgery in this group after 6 weeks. The fissure healing rate with open partial lateral internal anal sphincterotomy was

95.5%, whereas that for 0.2% nitroglycerin was 62% ($p = 0.0001$), which is comparable to previous studies, in which the healing rate with open partial lateral anal sphincterotomy was reported to be 94–100% [11-13]. Richard et al. [14] concluded that surgical sphincterotomy improved healing rate at 6 weeks (89% vs. 29%) and reduced the further requirement for surgery (3% vs. 89%) in his trial of 82 patients. With regard to symptoms, pain persisted in 26 (40%) patients treated with 0.2% nitroglycerin, whereas only two patients (3.4%) treated surgically complained of persistent pain because of abscess. Similarly, bleeding per rectum persisted in 15 patients (47%) who applied nitroglycerin ointment. By contrast, no bleeding per rectum persisted among those treated surgically. Incontinence of flatus as a complication of the procedure was reported in only one (1.5%) patients treated surgically, which is a result similar to that reported in previous studies [15,16]. One might argue that a more objective measure such as anal manometry should have been performed to assess anal sphincter status; however, we felt that the clinical symptom status was more relevant. Although this study suggests that continence is not adversely affected in the short term, further prospective evaluation with a comparison of control groups is needed to determine the long-term effect. Different studies showed high rate of headache with 0.2% nitroglycerin, but in our study it was 40%, which was controlled by simple analgesics [15,16]. A mean healing period of 3 weeks was observed in Group B, whereas for Group A it was 6 weeks, which was similar to that achieved by Coher A [11], Gorfine [7], and Lund and Scholefield [9].

Conclusion

This prospective clinical controlled study demonstrates that open lateral internal anal sphincterotomy is superior to the topical application of 0.2% nitroglycerin ointment in the treatment of anal fissure, with the advantages of good symptomatic relief, high rate of healing, fewer side effects, and a very low rate of early continence disturbances although topical application of GTN ointment for chronic anal fissure is safe with acceptable rate of healing of fissure can be achieved without risk of incontinence, but symptomatic relief of pain occurs at a slower rate than lateral sphincterotomy. It may have considered as a satisfactory first line option in treatment of chronic anal fissure.

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