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A Comparative Study of Topical Glyceryl Trinitrate and Lateral Sphincterotomy in Treatment of Chronic Anal Fissure

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Abstract:

Background: An anal fissure is a longitudinal tear or defect in the skin of the anal canal distal to the dentate line. An anal fissure is one of the most painful conditions encountered in surgical practice and causes considerable morbidity and reduction in quality of life. **Aims:** We aim to compare the efficacy of topical Glyceryl Trinitrate (GTN) versus lateral internal sphincterotomy (LIS) in the treatment of chronic anal fissure. **Patients and Methods:** This is a randomized clinical study carried out on consecutive patients who attended the surgery outpatient clinics at four hospitals in Sana'a City during the period of a year and a half (from October 2019 to April 2021). This study included 60 patients divided into two groups of 30 patients each. One study group was treated with topical application of 0.2% GTN, while another study group was subjected to LIS and all 60 patients were followed for a period of 6 weeks and observed. **Results** Among all the 60 patients (34 females, 26 males) all patients had come with complaints of pain. A total of 45 (75%) patients had pain with constipation, whereas 33 (55%) patients had bleeding per rectum along with pain. On clinical examination tenderness was elicited in all 60 patients, hypertonic anal sphincter elicited in 44 (73.3%), sentinel skin tag was noted in 18 (30%) patients. Group A included 30 (13 males, 17 females) patients treated with topical GTN ointment and group B included (13 males, 17 females) patients who underwent LIS. In group A, 26 patients were treated successfully but 4 patients were uncured. By contrast, all patients in group B were successfully treated (29) patients and only one (3.33%) patient came with unexplained discomfort, and 2 (6.67%) patients suffered from flatus incontinence. **Conclusion:** Despite good response to topical GTN treatment, it seems that LIS is more effective in the treatment of anal fissure with a high rate of healing, good symptomatic relief and very low rate of early incontinence. Medical treatment by GTN can be considered as a satisfactory first-line option in chronic anal fissure treatment.

Keywords: Anal fissure, Glyceryl Trinitrate, Lateral Internal Sphincterotomy, Sana'a, Yemen.

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Introduction

An anal fissure is known as a longitudinal tear or defect in the skin of the anal canal distal to the dentate line. Anal fissures are classified based on causative factors. Primary fissures are usually harmless and are likely to be related to local trauma such as prolonged diarrhea, hard stools, vaginal delivery or repetitive injury. Secondary fissures are found in patients with previous anal surgical procedures, inflammatory bowel disease (e.g. Crohn's disease), granulomatous diseases (e.g. tuberculosis, sarcoidosis), infections (e.g. HIV/AIDS, syphilis) or malignancy⁽¹⁾. An acute anal fissure commonly heals with 4–8 weeks of conservative treatment. If this therapy fails and the fissure becomes chronic, surgical intervention is usually required⁽²⁻⁴⁾.

Majority of fissures are acute and resolve within 6-8 week with conservative treatment. Chronic anal fissures are associated with hypertonia of the anal canal and reduction in mucosal blood flow, with microcirculatory disturbance and a poor healing tendency^(5, 6).

An anal fissure typically causes episodic pain that occurs during defecation and persists for 1-2 hours afterward⁽⁷⁾. 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⁽⁸⁾. The classical presentation is anal pain during or after defecation accompanied by the passage of bright red stool. In addition, purities ani may occur in up to 50% of cases⁽⁹⁾. Subcutaneous internal sphincterotomy remains the golden standard for the management of chronic anal fissure because of its simplicity, rapid healing, and low recurrence rate. Disadvantages of internal sphincterotomy include; disturbance of continence, bleeding, fistula, abscess, persistent wound pain, cost and time of recovery⁽¹⁰⁾.

These have led to search for another mode of therapy or pharmacologic way to create a temporary or reversible sphincterotomy, one that would lower the sphincter pressure only until the fissure healed⁽¹⁾. Local GTN can reduce the increased anal canal pressure caused by the hypertonic internal anal sphincter and improve the anodermal blood flow, as the surgical internal sphincterotomy do. Reversible chemical sphincterotomy produced by local GTN could be used to enhance healing of the anal fissure with minimal side effects thus avoid the need for operative intervention⁽¹¹⁾.

An anal fissure is the most common cause of severe anorectal pain in adults, contributing significantly to coloproctology workloads⁽¹²⁾. It is one of the most common lesions to be considered in

the differential diagnosis of anal pain, and typically causes episodic pain that occurs during defecation and persists for hours afterward⁽⁷⁾. Also, an anal fissure is a common problem that causes significant morbidity⁽¹³⁾.

As our knowledge, no systematic research has so far been conducted in Yemen to investigate differences between surgical and medical treatment of anal fissure, and assess efficacy of GTN, so this study was conducted to fulfill the gap of research on this topic in our local area.

Patients and Methods

This is a randomized clinical study included patients with chronic anal fissure, aged between 15 years and 65 years and who agree to participate were included in this study. Pregnant women, patients with acute anal fissure, recurrent anal fissure, inflammatory bowel disease, systemic diseases (diabetes mellitus, chronic liver disease and collagen diseases), hemorrhoids and those who under treatment with nitrates for other diseases were excluded from analysis. During the period of a year and half (from October 2019 to April 2021), this study was carried out on consecutive patients who attended to the surgery outpatient clinics at four hospitals in Sana'a City. Two hospitals were public hospitals (Kuwait and Republican hospitals), while two other hospitals were private hospitals (Azal and University of Science and Technology hospitals). Patients with chronic anal fissure were diagnosed clinically and divided up into two groups of 30 patients each. A topical 0.2 percent GTN was used in one trial group therapy along with a sitz bath.

Oral antibiotics such as Cap Amoxycillin 500 mg BD and Tab. Metronidazole 400 mg TDS were used during the first one week along with topical 0.2 percent GTN application about the size of a pea, over the anal edge thrice per day for a period of 6 weeks and observed. Another study group was subjected to LIS and followed also for a period of 6 weeks and observed. All patients were subjected to full detailed history stressing on symptoms of anal fissure including itching, bleeding, anal pain during and after defecation, and discharge. Possible cause of anal fissure as history of constipation and anal trauma were also reported. Digital rectal examination was to assess spasm and tenderness. The presence of linear ulcer in the distal anal canal, indurations, and sentinel skin tag, with the previous symptoms were enough for clinical diagnosis. Chronic anal fissure is diagnosed if the duration of the symptoms (pain–bleeding) was over 6 weeks with fibers of the internal anal sphincter visible at the base of the fissure. A verbal informed consent was obtained from all participants, covering the

study and publication of results, and they were informed about the nature of the study and the confidentiality of the study subjects was maintained. Moreover, this study was conducted in accordance with the Declaration of Helsinki.

Statistical analysis

All variables data were entered and organized into Excel software. A packaged computer analysis program, statistical package for the social science (SPSS 26.0, IBM Corp., Armonk, NY, USA) was used for statistical analysis of this data. A Shapiro–Wilk test confirmed that all the data were not normally distributed. Therefore, patients' age was stated as the median associated with the 25th to 75th percentile interquartile range (IQR). Chi-square test was used to compare between categorical variables; whenever any of the expected values were less

than 5, Fisher's exact test was used instead. All used statistical tests were performed at a 5% level of significance.

Results

Sixty patients were enrolled in this study. They were divided into two groups. Group (A) were treated by local 0.2% GTN ointment, while group (B) were treated by surgical intervention of anal fissure with LIS. As shown in table 1, majority of patients were females with distribution 36 (60%), while there were 24 (40%) patients were males, and female to male ratio was 3:2. Regarding age of patients, median age was 33.5 years (IQR =27.25-44, range = 18-61) years. The distribution of anal fissure patients in age groups (15-25), (26-35), (36-45), (46-55), and (56-65) years was 10 (16.7%), 23 (38.3%), 16 (26.7%), 7 (11.7%) and 4 (6.7%) patients respectively.

Table 1: Demographic characteristic of all patients

Demographic characteristic	Frequency (F)	Percentage (%)
Gender		
Male	24	40
Female	36	60
Age (Years)		
15-25	10	16.7
26-35	23	38.3
36-45	16	26.7
46-55	7	11.7
56-65	4	6.7

As shown in figure 1, constipation was found in 45 (75%) patients, and only 15 (25%) did not have any history of constipation.

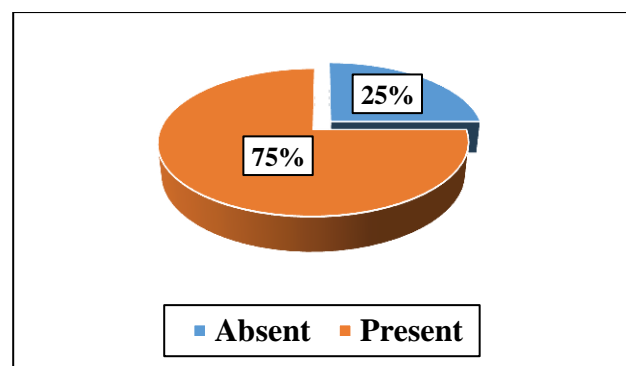


Figure 1: Distribution of constipation among all chronic anal fissure patients

Among group (A) patients, 17 (56.7%) were female, and the others 13 (43.3%) patients were males. Median age was 34 years (range = 18-61) years. All

group (A) patients (100%) presented with anal pain, while those patients who presented with anal pain and bleeding were 15 (50%) patients. By the end of 2nd, 4th and 6th weeks of follow-up, only 4 (13.3%), 15 (50%), and 29 (96.7%) patients had adequate pain improvement respectively, while 4 (13.3%), 9 (30%), and 24 (80%) had adequate optimal healing of fissure respectively.

Among group (B) patients, 19 (63.3%) were female, and the others 11 (36.7%) were males. Median age was 33 years (range = 23-60) years. All group (B) patients (100%) presented with anal pain, while those patients who presented with anal pain and bleeding were 19 (63.3%) patients. By the end of the 2nd, 4th and 6th weeks of follow-up, 12 (40%), and 23 (76.6%), and 30 (100%) patients had adequate pain improvement respectively, while 6 (20%), 27 (90%), and 29 (96.7%) patients had adequate optimal healing of fissure respectively.

In group (B), the rate of pain improvement was significantly higher than group (A) at 2 weeks (p -value = 0.020), and at 4 weeks (p -value = 0.030), but at 6 weeks, there were no significant differences between both groups (p -value = 0.500).

Group (B) showed significantly higher than group (A) towards optimal healing at 4 weeks (p -value = 0.000), however there were no significant differences between both groups at 2 and 6 weeks (p -value = 0.365, and 0.051 respectively). See table 2.

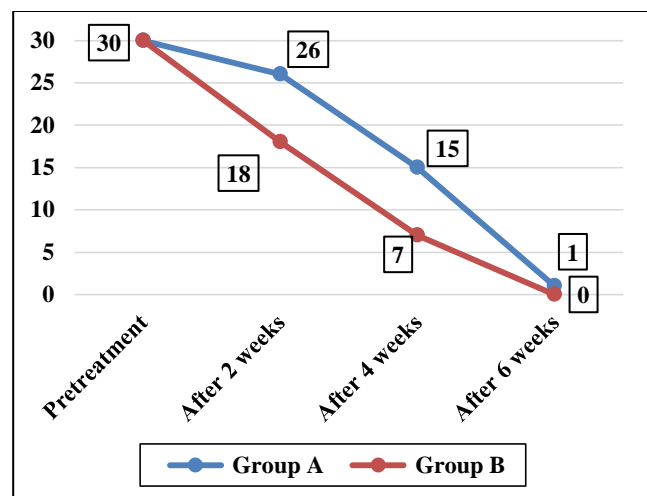


Figure 2: Pain improvement comparison between both groups

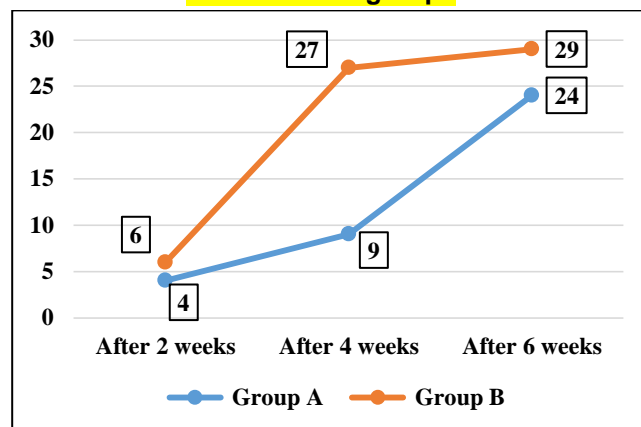


Figure 3: Optimal healing of the fissure comparison between both groups

Table 2: Outcomes of treatment in both groups during follow up period.

	At 2 weeks			At 4 weeks			At 6 weeks		
	Group A (0.2% GTN) (n= 30)	Group B LIS (n= 30)	p-value	Group A (0.2% GTN) (n= 30)	Group B LIS (n= 30)	p-value	Group A (0.2% GTN) (n= 30)	Group B LIS (n= 30)	p-value
Improved pain	4 (13.3%)	12 (40%)	0.020*	15 (50%)	23 (76.7%)	0.030*	29 (96.7%)	30 (100%)	0.500
Optimal healing	4 (13.3%)	6 (20%)	0.365	9 (30%)	27 (90%)	0.000*	24 (80%)	29 (96.7%)	0.051

Discussion

As our knowledge, this study is a first study that investigated between differences in both medical and surgical management for a chronic anal fissure treatment in Yemen, which makes it difficult to compare at local level.

Anal fissure is a common and painful anal canal illness. This disease's etiology is currently unknown.

However, it is thought to be caused by internal sphincter hypertrophy and increased anal sphincter resting pressure, leading in anoderm ischemia⁽¹⁴⁾. Majority of chronic anal fissure patients have elevated resting anal pressures caused by hypertonicity of the internal anal sphincter and this appears to play a role in anal fissure pathogenesis. Also, as there is a relative hypoperfusion at the

posterior commissure of the anal canal in most people, local ischemia may be important⁽¹⁵⁾.

Decrease the anal hypertonia, which may lead to heal the fissure by improve the anodermal blood flow is the main aim of the treatment.

For a long time, internal sphincterotomy was the gold 'standard' in therapy, producing immediate symptom relief and healing rates of more than 90%, but it is now less common as troubles in continence can occur in up to 30% of patients⁽¹⁶⁾. As a result, non-surgical options for lowering resting anal pressure and healing the fissure without jeopardizing anal continence were sought⁽¹⁷⁾.

Recognition of organic nitrates as the non-adrenergic, non-cholinergic neurotransmitter mediating relaxation of the internal anal sphincter has initiated the widespread use of organic nitrates in the treatment of chronic anal fissure. These agents are metabolized at a cellular level to release NO which, in turn, mediate relaxation of the internal anal sphincter by increasing cGMP level within the smooth muscle cells⁽¹⁸⁾.

Current study data showed slightly high number of female patients presenting with chronic anal fissure. This is inconsistent with most other studies^(13, 19-21). Constipation that is more common among females during pregnancy, as well as birth weight of the child, the time elapsed during the termination of pregnancy and perianal diseases might be the culprits^(22, 23).

Current study patients present 3.5 years younger than their Egyptian counterparts⁽²⁴⁾. Majority of the patients was found in between (26-35) years in both groups according to current study results. This is consistent with most other studies, and this age group appears to be higher predilection for chronic anal fissure development in ano^(13, 21, 24-28).

Constipation was reported in 75% in patients according to current data. In India constipation was (52.7%), Egypt (70%), Pakistan (71.7%) and Turkey (62.3%) as showcased in^(13, 19, 21, 24) respectively. Constipation is the most common medical complaint in the khat users^(29, 30), therefore this might interpret the slight increase of constipation among current study patients.

On the other hand, both techniques are useful treatment of chronic anal fissure according to current study results.

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Not surprisingly, patients who underwent sphincterotomy relieve pain much earlier as compared to GTN, as this result have been previously reported by other studies^(13, 19-21, 24), and after 6 weeks of treatment, pain relief in the two groups was comparable. In Egypt, *El-Labban et al.*, reported same results, but after 4 weeks only of treatment⁽²⁴⁾.

Optimal healing in LIS patients was also much earlier as compared to GTN according to current study results, but after 4 weeks of treatment only, however after 6 weeks, this advantage was disappeared. Normally by the end of the 2nd week of treatment, there is no complete healing of fissure in both groups. *El-Labban et al.*, reported this initial advantage was lost by the end of the 8th week⁽²⁴⁾. According to current study results, only one (3.3) patient had incontinence of flatus post sphincterotomy. Post sphincterotomy incontinence rate variedly between 0%-53%⁽³¹⁾.

Limitations

Like any study, this study has several limitations that must be acknowledged. Firstly, patient follow-up was done only for the first 6 weeks after the treatment, which was not enough to reflect any long-term results or recurrence of the symptoms. Secondly, the role of GTN ointment in recurrence cases was not investigated. Finally, current study does not reflect what is happening in other hospitals in Sana'a City or other governorates in Yemen, so the findings should be generalized cautiously.

Conclusion

Despite good response to topical GTN treatment, it seems that LIS is more effective in treatment of anal fissure with high rate of healing, good symptomatic relief and very low rate of early incontinence. Topical GTN treatment is one of choices in patients who are not willing to subject to surgery and/or not suitable for surgery. Further studies for longer duration of follow up are required.

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