

CHRONIC FISSURE IN ANO: 0.25% GLYCERYL TRINITRATE VERSUS LATERAL INTERNAL SPHINCTEROTOMY

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ABSTRACT

Objective: Chronic anal fissure is a painful linear tear at the anal verge distal to dentate line. Different options are available for its treatment. The objective of this study was to compare topical 0.25% Glyceryl Trinitrate with Lateral internal sphincterotomy for the treatment of chronic anal fissure in terms of healing, pain relief, complications of the treatment and recurrence of fissure.

Method: This Prospective Randomized controlled trial was carried out at Naseer Teaching Hospital, Gandhara University, Peshawar from 1st January 2013 to 31st July 2013. Patients were selected by simple random sampling technique and divided into Group 1 – Glyceryl trinitrate and Group 2 – Lateral Internal Sphincterotomy. Patients were followed up at 2, 4, 6 and 12 weeks. Data was analyzed on SPSS 17.

Results: The study included 80 patients; 37 in group 1 and 43 in group 2. Decrease in Visual Analogue Scale (VAS) pain score of ≥ 45 mm from the baseline was observed in 81.08% in group 1 at 12 weeks. Group 2 had decrease in VAS score in 86.04% within 48 hrs of surgery and in 97.6% at 12 weeks (p value <0.05). Anal fissure healed in 64.86% in group 1 and in 97.6% in group 2 (p value <0.05). Headache (62.16%) was the commonest complication in group 1. Transient gas and liquid incontinence were noted in 4.65% in group 2. Recurrence occurred in 32.43% in group 1 and 4.65% in group 2 (p value <0.05).

Conclusion: Lateral internal sphincterotomy is a safe procedure with minimal complications. It allows rapid pain relief and superior healing compared to Glyceryl trinitrate.

Key Words: Chronic anal fissure, Glyceryl trinitrate, Sphincterotomy.

INTRODUCTION

Anal fissure is a linear tear in the anal verge distal to the dentate line. Anal fissure can be either acute or chronic. Acute anal fissure is superficial and has minimal induration. If the fissure fails to heal for more than six weeks it is termed chronic.¹ Chronic anal fissure (CAF) has indurated margin and fibers of internal sphincter may be visible in the base of ulcer. Sentinel anal tag and hypertrophic anal papilla are also associated with CAF.¹

Different theories exist about the etiology of anal fissure. Increased resting anal pressure caused by increased internal sphincter tone causes ischemia of the anoderm, resulting in anal fissure.¹ Anal fissure commonly occurs in the posterior midline, which is the water shed area of blood supply. In 10-20 % females and 1-2% males anal fissure is seen in anterior midline.² Different treatment modalities are used to treat CAF with varying success. Treatment options range from pharmacological agents like topical Glyceryl trinitrate, Isosorbide dinitrate, Diltiazem, Botulinum toxin to surgi-

cal intervention such as anal dilatation, Lateral internal sphincterotomy, fissurectomy, anal advancement flap.^{2,4}

Treatment aims to reduce the resting anal pressure and improve the blood flow to anodermal area and allowing healing of fissure.² Nitric oxide is an important mediator of internal sphincter relaxation.^{1,2} Many authors have reported successful healing of anal fissure with Nitric oxide donors like Glyceryl trinitrate (GTN), isosorbide dinitrate. 2-4 Lateral Internal sphincterotomy (LIS) is a commonly performed procedure for the treatment of CAF. The objective of this study was to compare topical 0.25% GTN with LIS for the treatment of CAF in terms of fissure healing, pain relief, complications of the treatment and recurrence of anal fissure.

METHOD

This Prospective Randomized controlled trial was carried out at Naseer Teaching Hospital, Gandhara University, Peshawar from 1st January 2013 to 31st July 2013. The study was approved by the ethical review board of the institution.

All patients of either gender, between 18 and 70 years with CAF were included in the study. Written informed consent was given by all the patients. Patients were advised to discontinue any NSAIDs, Paracetamol and other analgesics for the duration of study. The study excluded patients with associated hemorrhoids, anal

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fistula, perianal abscess, anal stenosis, anal malignancy, previous anal surgery, pregnancy, uncontrolled diabetes mellitus, migraine or chronic headaches, patients on nitroglycerine e.g. ischemic heart disease, patients on phosphodiesterase 5 inhibitor and anal fissure due to an underlying condition e.g. tuberculosis, inflammatory bowel disease.

Study units were selected by simple random sampling technique using sealed envelopes. Sealed envelopes containing the group number (Group 1: 0.25% GTN, Group 2: Surgery) were kept in the basket in equal proportion and patients were asked to select one sealed envelope. All the patients were assessed in the out patient department. Detailed history and thorough physical examination were carried out.

Patients in Group 1 (Glyceryl Trinitrate Group) were advised to apply pea sized GTN 0.25% paste at the anal verge and anal fissure with cotton bud three times a day for twelve weeks.

Patients in group 2 were admitted on the day of surgery. One dose of intravenous third generation Cephalosporin (1 gram) and Metronidazole (500 milligram) was administered at the time of induction of anesthesia. Surgery was performed under General anesthesia with endotracheal intubation. A small incision was made over the intersphincteric groove, fibers of internal sphincter were separated from external sphincter and anal mucosa. Distal 1 cm of internal sphincter was grasped in Allis' forceps and cut with scissors under vision. Any anal tag was also excised. Bleeding was controlled by digital pressure.

Postoperatively, patients were shifted to the ward and monitored for the development of any complications. Patients were discharged on the first postoperative day, if stable. Patients were advised daily hot soaks and laxatives. Patients in both the groups were followed up at two, four, six and twelve weeks.

Important variables of the study were: Post treatment decrease in VAS score, healing of fissure, local complications of LIS, complications of topical GTN and recurrence of fissure.

Healing of fissure was defined as complete epithelialization of fissure.

Fecal incontinence was evaluated by Wexner score. Wexner score considers three types of incontinence (solid, liquid, gas); it also includes the need to wear a pad and effect on life style. Frequency of each of these factors is given a score from zero to four. The total score ranges from 0 (complete continence) to 20 (complete incontinence).

Post-treatment pain was assessed by VAS. Patients were asked about the intensity of their pain after

surgery and during follow up. VAS consisted of a 100-mm horizontal line marked at one end with the words "no pain" and at the other end with the words "worst pain imaginable." The researcher asked the patients to mark the line at the point that best represented the intensity of their pain. The VAS numeric value was the distance in millimeters from "no pain" to the point marked by the patient.

The data was collected on a structured proforma and analyzed on SPSS 17. Mean, standard deviation were used for continuous data while frequency and proportions for categorical or dichotomous data. Tests of significance included independent sample T test for continuous or discrete data and Chi-square test for categorical or dichotomous data. 95% confidence interval was used. P value of less than 0.05 was considered significant.

RESULTS

The study included eighty patients; thirty seven in group 1 (Topical GTN) and forty three in group 2 (LIS).

Patients' demographic data, symptoms and fissure characteristics are given in table I. Patients' age, gender, symptoms and anal fissure characteristics were similar between the two groups.

Pre-treatment Pain score on VAS was ≥ 70 mm in 62.16% (n=23) in group 1 and 65.11% (n=28) in group 2 (p value >0.05). Mean VAS score before treatment was 65.03 mm (SD ± 18.34) in group 1 and 71.77 mm (SD ± 14.48) in group 2 (p value >0.05). Detail of pre-treatment VAS score is in table I.

Decrease in VAS score of ≥ 45 mm from the baseline was observed in 81.08% (n=30) in group 1 at 12 weeks. Group 2 had decrease in VAS score in 86.04% (n=37) within 48 hrs of surgery and in 97.6% (n=42) at 12 weeks. Details of pain relief are in table II.

Anal fissure healed in 64.86% (n=24) at 12 weeks in group 1; healing of anal fissure was observed in 97.6% (n=42) in group 2 (p value <0.05). Those who did not respond to GTN were managed by LIS. Detail of fissure healing is in table II.

Commonest complication in group 1 was headache in 62.16% (n= 23). Headache responded to oral Paracetamol. Four patients discontinued GTN because of severe headache. Other complications noted in group 1 were: dizziness due to orthostatic hypotension in 8.10% (n=3), palpitations 2.7% (n=1), perianal pruritis in 5.41% (n=2).

Transient gas and liquid incontinence (mucus leak) was noted in 4.65% (n=2) after surgery; it improved within two months. Wound infection occurred in 4.65% (n=2); it resolved with antibiotics. There was no mortality in this study.

Table I: Base Line Features

S.No.	Variables	Group 1		Group 2		P value
1.	Age (yrs) mean	36.64yrs (SD±4.93)		38.06yrs (SD±5.1)		>0.05
2.	Gender	F: 17	M: 20	F: 20	M: 23	>0.05
3.	Bleeding from fissure	n=34	91.89%	n=40	93.02%	>0.05
4.	Constipation	n=36	97.29%	n=41	95.35%	>0.05
5.	Baseline anal pain (VAS) mean	65.03mm (SD±18.34)		71.77mm (SD±14.48)		>0.05
6.	Baseline VAS score: ≤49mm	n=2	5.41%	n=1	2.33%	>0.05
7.	Baseline VAS score ≥50-69mm	n=12	32.43%	n=14	32.56%	>0.05
8.	Baseline VAS score: ≥70mm	n=23	62.16%	n=28	65.11%	>0.05
9.	Anterior midline anal fissure	n=10	27.03%	n=13	30.23%	>0.05
10.	Posterior midline anal fissure	n= 23	62.16%	n=26	60.47%	>0.05
11.	Both anterior & posterior midline	n=4	10.81%	n=4	9.30%	>0.05
12.	Sentinel anal tag	n=33	89.19%	n=39	90.69%	>0.05

Group 1: Topical Glyceryl Trinitrate Group

Group 2: Lateral Internal Sphincterotomy Group.

VAS: Visual Analogue Scale.

SD: Standard Deviation

M: Male, F: Female

Table II: Detail of Important Variables

S.No.	Variables	Group 1		Group 2		p value
		number	%	number	%	
1.	Pain relief at two weeks	19	51.35	37	86.04	<0.05
2.	Pain relief at six weeks	25	67.57	39	90.69	<0.05
3.	Pain relief at twelve weeks	30	81.08	42	97.67	<0.05
4.	Control of bleeding from fissure	27	72.97	42	97.67	<0.05
5.	Healing of fissure at six weeks	10	27.02	37	86.04	<0.05
6.	Healing of fissure at twelve weeks	24	64.86	42	97.67	<0.05
7.	Recurrence of fissure	12	32.43	2	4.65	<0.05

Group 1: Topical Glyceryl Trinitrate Group

Group 2: Lateral Internal Sphincterotomy Group.

DISCUSSION

Anal fissure is a common anal condition and causes considerable morbidity. Most patients present with severe pain during or after defecation and passage of fresh blood per anus.

Different treatment options are available for anal fissure. Each has its merits and de-merits. Conservative measures like topical analgesics, laxative and sitz baths may be able to heal majority of acute anal fissures but only 8 - 51% CAF respond to conservative treatment.²

Many authors have recommended topical GTN as a first line treatment for CAF because of its ease of use, safety, non-invasiveness and cost effectiveness.^{4,5} Topical GTN is a nitric oxide donor. It acts on the internal anal sphincter and decreases its tone, allowing healing of anal fissure.^{2,4,6} Adequate healing of fissure requires

GTN application for more than six weeks and in some cases up to twelve weeks.⁴ In our study topical GTN achieved healing of fissure in 64.86% (n=24); healing rate improved from 27.02% at six weeks to 64.86% at twelve weeks. This result is consistent with other studies.^{5,9}

Higher concentration of topical GTN up to 0.4% achieves higher healing rate but at the cost of higher frequency of side effects especially headache.¹⁰ A randomized double blind placebo controlled trial was conducted by Berry SM et al; they compared 0.4% GTN with placebo for pain associated with CAF. ¹⁰ In that study headache occurred in 69.9% compared to 47.6% in placebo group and 5.7% cases had to discontinue GTN because of severe headache. In our study headache was noted in 62.16%. This is comparable with other studies.^{5,9,11} A randomized study compared

perianal with endoanal 0.4% GTN application for CAF; the authors reported that endoanal GTN application resulted in significantly lesser frequency of headaches and higher healing rate compared to perianal GTN application.¹²

Many authors have suggested that decrease in anal sphincter pressure is temporary and fissure may recur after healing. Recurrence rate is up to 57% with GTN.¹³ In our study recurrence was noted in 32.43% after successful healing. Nelson RL et al in Cochrane Database Review reported 'GTN is marginally but significantly better than placebo but late recurrence of fissure is common, in the range of 50% and that all medical therapies are less effective than surgery for the treatment of chronic anal fissure'.¹⁴

LIS is the most common procedure performed for CAF. It allows rapid symptom relief and higher healing rate compared to GTN. LIS allows healing of fissure in up to 100% patients.¹⁵ In our study fissure healed in 97.67%. This result is consistent with other studies.^{15,18} A study by Rather SA et al, reported 100% healing of fissure with LIS compared to only 56.9% with GTN.¹⁵ The authors concluded that LIS was safe with highest patient satisfaction and more curative than GTN, and that LIS should be used as first line treatment for chronic as well as recurrent acute anal fissures.¹⁸

Recurrence after LIS ranges from 0 – 15.4%.¹ In our study two patients had recurrence. Duration of follow up in our study was short so recurrence could not be assessed properly.

A major drawback of LIS is faecal incontinence that ranges from flatus incontinence to complete inability to control faeces. Various authors have reported 3.3 - 16 % incontinence rate after LIS.^{1,19,20} Most cases of incontinence are transient and improve within two months time.¹ Incontinence rate beyond two months ranges between 3 to 7%.¹ Risk of incontinence depends on the extent of sphincterotomy.¹⁹ A study by Jaleel F et al compared conservative LIS with Topical GTN application. The authors divided the internal sphincter to one cm in contrast with the standard sphincterotomy in which the internal sphincter is divided up to the dentate line. The authors had temporary incontinence to mucus and flatus in 2.98%.¹⁹ A study by Murad-Regadas SM et al assessed the safe length of sphincterotomy in women with CAF. The authors suggested that the safe extent of division was less than 25% of the total sphincter length, which in women corresponded to less than 1 cm.²⁰ Other authors have also reported low risk of incontinence with conservative sphincterotomy ranging between 0.4 – 3.7%.²¹

In short, LIS allows rapid symptom relief and superior healing compared to GTN. This is especially beneficial in our setup where majority of patients are underprivileged, belong to far-flung areas; they demand rapid symptom relief and are usually non-compliant to

long medical treatment.

This was the first study performed at our institute on this topic. There were many limitations in the study; some of these were: short follow up, small sample size and no manometric analysis of anal sphincter.

CONCLUSION

LIS is a safe procedure with minimal complications. It allows rapid pain relief and higher healing compared to GTN.

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