

# COST EFFECTIVENESS OF TOPICAL GLYCERYL TRINITRATE VERSUS LATERAL INTERNAL SPHINCTEROTOMY FOR CHRONIC ANAL FISSURE

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## ABSTRACT

**Objective:** To compare the cost effectiveness of initial use of topical glyceryl trinitrate (GTN) before lateral internal sphincterotomy against the sphincterotomy as primary treatment modality for chronic anal fissure.

**Material and Methods:** This prospective randomized study was conducted at Isra University Hospital, Hyderabad between November 2004 and October 2005. Fifty patients fulfilling the criteria were randomised into two equal groups. One group was treated with topical GTN ointment and other group with lateral internal sphincterotomy. Patients were followed up for one year. In case of failure of treatment or recurrence in GTN group, the patients were subjected to lateral sphincterotomy. The total expenditures of treatment in both groups were separately calculated and compared.

**Results:** Pain relief was observed in 92% of the patients in both the groups after 6 weeks. Complete healing of fissure was observed in 92% and 88% of the patients in GTN group and sphincterotomy group respectively after 6 weeks. Recurrence was observed in 16% of the patients in GTN group and none in sphincterotomy group after one year. The sphincterotomy was avoided in 76% of the patients in GTN group during one year. The total expenditure of GTN group was Pakistani Rupees (PKR) 139500 and of sphincterotomy group was PKR 387500; about 2.8 time the expenditure of GTN group.

**Conclusion:** The initial use of topical GTN before sphincterotomy against the sphincterotomy as primary treatment modality for chronic anal fissure is cost effective and provides substantial monetary benefit.

**Key words:** Anal fissure, GTN, Internal sphincterotomy, Cost effectiveness.

## INTRODUCTION

Anal fissure is an extremely painful condition characterized by a linear tear in the lower anal canal below the dentate line. Its classical features are painful defaecation, bright red per rectal bleeding and constipation. Anal fissures are most commonly seen in the posterior midline, although 10-20% in women and 1-10% in men are located in the anterior midline<sup>1</sup>. Various treatment modalities have been employed with variable success rates. The initial modality of manual dilatation is considered obsolete due to irreversible damage of sphincter mechanism with incontinence rates reported over 50% at extended follow up intervals over 15 years<sup>2</sup>. The lateral internal sphincterotomy is considered gold standard surgical procedure nowadays but the incontinence

is most important complication reported with this operation. Besides this surgical procedure, the successful use of glyceryl trinitrate (GTN) in the treatment of anal fissure has substantially increased in recent years. Topical use of GTN ointment reduces the spasm of internal anal sphincter and so relieves the pain of anal fissure.

The financial burden of various treatment options is being debated vigorously throughout the world. The issue of financial impact assumes far greater importance in the context of already overburdened economy especially in under developed countries. Its importance is further multiplied in countries devoid of support systems like National Health Service (NHS).

The objective of this study was to compare the cost effectiveness of initial use of

**PAIN RELIEF**

Treatment group	After 2 weeks	After 4 weeks	After 6 weeks
GTN group (n = 25)	11 (44%)	20 (80%)	23 (92%)
Lateral sphincterotomy group (n = 25)	18 (72%)	21 (84%)	23 (92%)

Table 1

**FISSURE HEALING**

Treatment group	After 2 weeks	After 4 weeks	After 6 weeks
GTN group (n = 25)	00 ( 0 )	08 (32%)	23 (92%)
Lateral sphincterotomy group (n = 25)	10 (40%)	21 (84%)	22 (88%)

Table 2

GTN ointment before sphincterotomy against the Sphincterotomy as primary treatment modality for chronic anal fissure.

**MATERIAL AND METHODS**

This is a prospective randomized cohort study carried out at Isra University Hospital, Hyderabad from November 2004 to October 2005. A total of 50 patients were included in this study after taking written informed consent and were randomly divided into two groups. Acute fissures (duration of less than 6 weeks) were not included in this study. Group A comprises of the patients, who were initially treated with 0.2% topical GTN ointment and group B comprises of the patients who were subjected to lateral internal sphincterotomy. Patients in group A were advised to apply 0.2% GTN ointment three times daily by using gloved finger. If complete pain relief and epithelialization was not achieved by 6 weeks or developed recurrence, then the patients were recommended to have lateral internal sphincterotomy. Group B patients were subjected to lateral internal sphincterotomy performed under general anaesthesia as day care procedure. Park's anal retractor was inserted and internal sphincter was stretched and made easily palpable. A small incision is then made on the lateral aspect of anal canal just below the internal sphincter. An intersphincteric plane was developed between anal skin and internal sphincter by using scissors and internal sphincter is then divided by scissors. Bleeding was controlled by firm finger pressure. Patients in both groups were prescribed to take stool softeners and isphagul husk. Patients were followed in out patient department at 2<sup>nd</sup> week, 4<sup>th</sup> week and 6<sup>th</sup> week followed by monthly intervals for about one year. During the follow up, patients were asked about pain relief and fissures were examined for healing. Complete absence of pain was considered as symptomatic pain relief while complete epithelialization of fissure was labeled as healed fissure. The total expenditures of treatment in both groups of patients were calculated separately and then the two expenditures were compared.

**RESULTS**

Fifty patients were divided in two equal groups. Both groups were comparable in age and duration of symptoms. All the patients presented with painful defaecation. Forty patients had bleeding per rectum along with hard stools. The mean duration of symptoms of these patients were 6 months (range 2 months to 10 months). Patients of both groups were followed up in OPD after 2<sup>nd</sup>, 4<sup>th</sup> and 6<sup>th</sup> weeks of treatment with main emphasis on pain relief and healing of fissure. Complete disappearance of pain was considered 'successful pain relief'. At the end of 2<sup>nd</sup> week, only 11 patients (44%) in group A (GTN group) had complete pain relief as compared to 18 patients (72%) in group B (Lateral internal Sphincterotomy group). This showed a prompt and early pain relief in patients who were subjected to sphincterotomy as compared to GTN. At the end of 4<sup>th</sup> week of treatment, there was minimal difference (4%) in pain relief in both groups and this difference disappeared completely at the end of 6<sup>th</sup> week. The pain relief with both modalities of treatment is shown in table 1. Fissure was labeled as "completely healed" when it was found completely epithelialized. At the end of 2<sup>nd</sup> week no patient in group A (GTN group) showed healing of fissure compared to 10 patients (40%) in group B (Lateral sphincterotomy group). During subsequent follow-up after 4<sup>th</sup> week, eight patients (32%) in group A showed complete healing of fissure as compared to 21 patients (84%) in group B. At the end of 6<sup>th</sup> week, in group A 23 patients (92%) showed fissure healing as compared to 22 patients (88%) in group B. The fissure healing with both modalities of treatment is shown in table 2. In group A (GTN group), five patients (20%) had some burning sensation at the site of application of GTN ointment and four patients (16%) had mild transient and tolerable headache which subsided itself over next few days (table 3). In Group B (Sphincterotomy group), nine patients (36%) had minor bleeding at operative site and this stopped spontaneously. Wound infection was seen in two patients (8%) and localized haematoma in one patient. Four patients (16%) had flatus

## COMPLICATIONS

Complications		GTN group (n = 25)	Lateral sphincterotomy group (n = 25)
Short Term complication	Bleeding	0 (0%)	9 (36%)
	Burning sensation	5 (20%)	0 (0%)
	Headache	4 (16%)	0 (0%)
	Flatus incontinence	0 (0%)	4 (16%)
	Wound Infection	0 (0%)	2 (8%)
	Localized haematoma	0 (0%)	1 (4%)
Long Term complication	Recurrence	4 (16%)	0(0%)

Table 3

incontinence which improved by itself in 34 months. None of the patients subjected to lateral sphincterotomy had faecal incontinence. In group B (sphincterotomy group), 16 patients had short term complications as compared to nine patients in group A (GTN group). During the follow up over a period of one year, 16% ( 4/25) recurrence rate was seen in Group A (GTN group) as compared to no recurrence in group B (sphincterotomy group). The four patients having recurrence underwent sphincterotomy. The total expenditure of Group A patients was about PKR 139500. The total expenditure of Group B patients was about PKR 387500. The details of expenditure are mentioned in table 4.

## DISCUSSION

Anal fissure is a linear tear in the mucosa of the anal canal normally extending distally from the dentate line to the anal verge. An acute tear in the mucosa is analogous to a "split lip" of the anus; if this fails to heal, it progresses to a chronic anal fissure.<sup>3</sup> Although there is no defined time period distinguishing acute from chronic fissures,

some authors suggest a chronic fissure should be present for at least 6-8 weeks.<sup>4,5</sup> High resting anal pressure caused by increased internal sphincter tone results in reduced blood flow of the mucocutaneous linings and leads to fissure.<sup>6</sup> Fissure tends to occur at the watershed of blood supply. i.e. the anterior and posterior midline in women and posterior midline in men. Multiple fissures or fissure occurring in lateral position arouse suspicion of the diseases like Crohn's disease, ulcerative colitis, tuberculosis, HIV infection etc. The maximum resting anal pressure (MARP) is raised in patients with anal fissure. A study with laser doppler flowmetry showed reduced blood flow at the posterior commissure of anal canal compared with that in the other three quadrants<sup>7</sup>. Anodermal blood flow is negatively correlated with resting anal pressure. When resting anal pressure falls under anaesthesia, a rise in anodermal blood flow is noted. After lateral sphincterotomy, there is a significant fall in resting anal pressure and a significant rise in anodermal blood flow.<sup>6</sup> This makes clear that ischemia plays an important part in pathogenesis of chronic anal

## FINANCIAL EXPENDITURE

Title of Expenditure	Amount (in Pakistani Rupees)
Average expenditure per patient for GTN treatment	1860
Average expenditure per patient for Sphincterotomy	15500
Total expenditure of 19 patients having successful GTN treatment without recurrence	35340
Total expenditure of 2 patients having failure of GTN treatment and requiring sphincterotomy subsequently	34720
Total expenditure of 4 patients having successful GTN treatment followed by recurrence and requiring sphincterotomy	69440
Total expenditure of Group A	139500
Total expenditure of Group B	387500
Expenditure per patient of Group A	5580
Expenditure per patient of Group B	15500

Table 4

fi ssure and also explains the presence of sphincter spasm, severe pain, predilection for posterior midline and poor healing.<sup>8</sup> Topical GTN ointment is the gold standard nonoperative treatment nowadays. Nitric oxide (NO) has been identified as the neurotransmitter responsible in mediating the relaxation of internal anal sphincter.<sup>9</sup> Topical GTN ointment rapidly reduces the resting pressure in the upper anal canal in normal subjects and patients with constipation.<sup>10</sup> Lateral internal sphincterotomy is the gold standard operative treatment for chronic anal fissure. The procedure may be performed using an open / closed technique and using local / general anaesthesia. Complications like bleeding, haematoma, abscess, non healing, persistent wound discharge, pruritis and faecal or flatus incontinence have been noted in different studies<sup>11,12</sup>. A study of 70 patients comparing topical GTN ointment and sphincterotomy with follow up of about 24 months<sup>13</sup> concluded that many anal fissures heal with topical GTN; lateral internal sphincterotomy remains effective but should be reserved for patients who fail to respond to initial GTN. Another study concluded that local application of GTN can avoid surgery in more than 80% of the patients with chronic anal fissure<sup>14</sup>. The choice of surgical vs chemical sphincterotomy as the initial treatment of choice for chronic anal fissure is at present controversial. The proponents of pharmacological therapy correctly note that a significant proportion of fissure patients are cured following this approach, often with no side effects, and without the cost, risk and inconvenience of surgery.

As this is a common disease, so the impact of choosing most appropriate treatment modality on overall economic resources is substantial. In a study<sup>15</sup> of 67 patients, a treatment algorithm from topical GTN to botulinum toxin (BTX) to lateral internal sphincterotomy was developed and it was concluded that this algorithm with stepwise escalation can avoid surgery in 88% of the patients. It was also concluded that this algorithm resulted in savings of 41% (compared with BTX plus sphincterotomy) and up to 70% (compared with sphincterotomy in all patients) respectively. In another study<sup>16</sup> based on decision tree model, it was concluded that the initial use of GTN compared to lateral internal sphincterotomy to treat a chronic anal fissure affords a potential cost reduction to the National Health Service (NHS) of Pounds 224 per patient without any loss in effectiveness.

The present study shows that in patients with chronic anal fissures, lateral internal sphincterotomy relieves pain much earlier as compared to topical GTN ointment. Pain relief was comparable after 4<sup>th</sup> week in both groups. Healing

was also found much earlier after lateral internal sphincterotomy than topical GTN, but after 6<sup>th</sup> week healing was more in GTN group as compared to lateral sphincterotomy group. The surgery was avoided in about 76% of the patients in GTN group during the follow up of about one year. The difference of expenditure between two groups of our study was about PKR 248000 and this means that the total expenditure of group B was about 2.8 times the expenditure of group A.

It is concluded that initial use of topical GTN before sphincterotomy against the sphincterotomy as primary treatment modality for chronic anal fissure is cost effective and provides substantial monetary benefit. It is also concluded that the initial treatment of chronic anal fissure should be with topical GTN because it is safe, well tolerated and pain relief & fissure healing rates are comparable with lateral internal sphincterotomy after 4-6 weeks of treatment. Lateral internal sphincterotomy should be reserved for patients with severe unrelenting pain as pain relief is much quicker as compared to topical GTN.

## REFERENCES

1. Notaras MJ. Anal fissure and stenosis. *Surg Clin North Am* 1988; 68: 1427-40.
2. Konsten J, Bacten CG. Hemorrhoidectomy vs. Lord's method: 17-year follow up of a prospective, randomized trial. *Dis Colon Rectum* 2000; 43: 503-6.
3. Steele SR and Madoff RD. Systematic review: The treatment of anal fissure. *Aliment Pharmacol Ther* 2006; 24: 247-57.
4. Corman ML. Anal fissures. In: Corman ML, ed. *Colon & Rectal surgery*, 5th edn. Philadelphia, PA: Lippincott Williams & Wilkins, 2005: 255-77.
5. Lindsey I, Jones OM, Cunningham C, Mortensen NJ. Chronic anal fissure. *Br J Surg* 2004; 91: 270-9.
6. Mishra R, Thomas S, Maan SM, Hadke NS. Topical Nitroglycerin versus lateral internal sphincterotomy for chronic anal fissure: Prospective, randomized trial. *ANZ J Surg* 2005; 75: 1032-5.
7. Schouten WR, Briel JW, Auwerda JJ. Relationship between pressure and anodermal blood flow. The vascular pathogenesis of anal fissure. *Dis Colon Rectum* 1994; 37: 72-9.
8. McCallion K, gardiner KR. Progress in the understanding and treatment of chronic anal fissure. *Postgrad Med J* 2001; 77: 753-8.
9. O'Kelly T, Brading A, Mortensen N. Nerve mediated relaxation of the human internal anal

- sphincter: role of nitric oxide. *Gut* 1993; 34: 689-93.
10. Guillemot F, Leroi H, Lone YC, Rousseau CG, Lamblin MD, Cortot A. Action of in situ nitroglycerin on upper anal canal pressure of patients with terminal constipation. A pilot study. *Dis Colon Rectum* 1993; 36: 372-6.
  11. Milito G, Arullani A, Brancalone C, Cesca D, Filingeri V, Casciani CU. Subcutaneous lateral internal sphincterotomy is the treatment of chronic anal fissure. *Ital J Surg Sci* 1983; 13: 275-9.
  12. Walker WA, Rothenberger DA, Goldberg SM. Morbidity of internal sphincterotomy for anal fissure and stenosis. *Dis Colon Rectum* 1985; 28: 832-5.
  13. Libertiny G, Knight JS, Farouk R. Randomized trial of topical 0.2% glyceryl trinitrate and lateral internal sphincterotomy for the treatment of patients with chronic anal fissure: Long term follow-up. *Eur J Surg* 2002; 168: 418-21.
  14. Oettle CG. Glyceryl trinitrate vs sphincterotomy for treatment of chronic anal fissure-in-ano: A randomized, controlled trial. *Dis Colon Rectum* 1997; 40:1318-20.
  15. Essani R, Sarkisyan G, Beart RW, Ault G, Vukasin P, Kaiser AM. Cost saving effect of treatment algorithm for chronic anal fissure: a prospective analysis. *J Gastrointest Surg* 2005; 9(9): 1237-43.
  16. Christie A, Guest JF. Modelling the economic impact of managing a chronic anal fissure with a proprietary formulation of nitroglycerin (Rectogesic) compared to lateral internal sphincterotomy in the United Kingdom. *Int J Colorectal Dis* 2002; 17(4): 259-67.

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