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# ANAL FISSURE;
## TREATMENT WITH GLYCERYL TRINITRATE (FIVE YEARS EXPERIENCE)

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**ABSTRACT... Objective:** To evaluate the efficacy of glyceryl trinitrate (GTN) preparation for the treatment fissure in-ano. **Design:** This study is a prospective clinical trial. **Place and duration:** this was conducted initially at PMC Faisalabad and other centers from November 2001 to onward for the period of five years. **Patients and Methods:** Out of 306 patients, 42 disliked/ refused this modality of treatment and was launched on 264 patients. 114 patients never followed up so, were excluded from the study. The remaining 276 patients applied 0.2% glyceryl trinitrate preparation on their anal verge thrice a day for two months. The patients were followed up at 1st to 12th weeks. The extent of improvement in the presenting symptoms, side effects and complications were noted on questionnaires. **Results:** A healing rate of 64.3%, and recurrence occurred in 35.7 %. 72 patients demanded surgery after failure/ non-compliance of GTN ointment treatment. **Conclusion:** glyceryl trinitrate preparation is a safe and effective modality for the treatment of fissure in-ano.

**Key words:** Fissure-in-ano, Constipation, Recurrence.

## INTRODUCTION

Fissure in-ano is a longitudinal tear in the lining of the distal anal canal, extending from dentate line to anal verge. It is a common proctologic problem affecting all age groups but seen particularly in middle-aged people[1]. About 90% fissure in-ano occur in posterior midline[1]. Fissure in-ano at lateral position is rare, but infectious diseases like syphilis, T.B., immunosuppressive diseases, inflammatory bowel diseases may be the cause. The usual complaints are pain on defecation (moderate to severe), constipation, bright red blood along the surface of stools, pruritis-ani and discharge per rectum. Many cases of acute fissure in-ano heal spontaneously but others enter into a vicious cycle of anal pain, constipation, faecal trauma and sphincter spasm[1,2,3,4,5,6].

The pathogenesis of chronic (more than 6 weeks) anal fissure is poorly understood[1,2]. The passage of a hard stool bolus traumatizes the anal mucosa. This is a possible initiating factor, but does not explain why only one in four patients report constipation. Increased tone of internal sphincter, ischaemia of ano-derm, obstetrics trauma, fibrosis and autoimmune diseases have been implicated[1,2,3,7,8,9].

Various conservative modalities have been implicated for the management of chronic fissure-in-ano[10,11,12,13,14] It has been documented that the topical application of glyceryl trinitrate (GTN) ointment heals chronic anal fissures and it is claimed to be an alternative to the traditional surgical interventions[2, 4,5,7,8,9,10,11,12,13]. Although the GTN reduces anal sphincter pressure significantly from the baseline and improves the blood circulation, high recurrence rate (25-43%) and headache has been reported with this modality of treatment[9,10,13,16,17,19,20].

This is an era of minimal invasive and cost effective approach. Conservative approaches are getting popularity. Surgical interventions like sphincterotomy was the "gold standard" many years back. Manual dilatation of the anus to lower the tension of internal anal sphincter was commonly practiced in past decades, which could lead to permanent sphincter injury and incontinence[2,6,14,15,,21]. Conservative measures like bulk laxative, stool softeners, local anesthetics, dicyclomine, calcium channel blocker, and botulinum toxin are also being used[7,9,10,13,19,20]. Although results of these modalities are encouraging, yet these are still to be studied more in our country.

## PATIENTS AND METHODS

A consecutive forty-six patients (Male 204, Female 70, Intersexes 2) suffering from fissure in-ano were included in a trial of GTN ointment at DHQ / Allied Hospital Faisalabad, since Nov. 2001, after taking written informed consent from each patient for the study.

Thorough history and clinical evaluation was performed. The diagnosis of chronic fissure in-ano was made on the basis of usual symptoms and presence of a tear in the long axis of lower anal canal, a sentinel tag of skin with indurations at the edges of the fissure by making the buttocks apart gently and the presence of symptoms for more than two months.

Further evaluation/ investigations carried out in suspected cases of secondary causes. A follow-up was done after 1,$^{st}$ 2,$^{nd}$ 4$^{Th}$ ,6$^{th}$ and 12$^{th}$ weeks. 0.2 % glyceryl trinitrate prepared in soft liquid paraffin was used. A pea-sized amount (0.5ml) was applied at the anal verge thrice a day.

Method of application was demonstrated to the patients on their first visit. Symptomatic relief from headache was achieved with Tab. Paracetamol. At follow-up, symptoms were assessed on a prescribed questionnaire and anus was examined for healing/ recurrence of symptoms.

## RESULTS

Mean age of patients was 30 years (range 16-58 years). Majority of patients (120) were falling in age group of 31-35 years. Male to female ratio in this study is about 3:1. Fissure in-ano was present at 6'O clock position (posterior anal fissure) in 89.3% patients and at 12'O clock (anterior anal fissure) in 10.7% of cases.

Pain on defecation was present in all patients, bleeding per rectum in 88.6%, discharge per rectum in 21.4% pruritus-ani in 21.4%, and sentinel pile was present in 85.7% of the patients.

Satisfactory relief of pain and healing of fissures were achieved in 64.3% of patients after about 12 weeks of treatment.

All patients treated by glyceryl trinitrate preparation complained of headache ranging from mild (71.4%) to moderate (28.6%). And 50 % patients used Tab. Paracetamol for symptomatic relief.

Compliance of patients to GTN preparation was also studied. Patients in urgency refused this modality of treatment due to prolong time required and un-predictability for healing.

| Table-I. Symptomatology of fissure -in-ano | | | |
|---|---|---|---|
| **Symptoms** | **No. Of patients** | | **%age** |
| Pain / discomfort on defecation | Mild<br>Moderate<br>Severe | 24<br>120<br>192 | 7<br>35.7<br>57.1 |
| Constipation | Absent<br>Mild<br>Moderate<br>Severe | 24<br>114<br>132<br>72 | 7.1<br>32.1<br>39.3<br>21.4 |
| Bleeding per rectum / staining of paper | Absent<br>Occasional<br>Mild | 72<br>216<br>54 | 21.4<br>64.3<br>14.3 |
| Discharge per rectum | Absent<br>Present | 264<br>72 | 78.6<br>21.4 |
| Pruritus-ani | | 72 | 21.4 |
| Sentinel pile | | 282 | 85.7 |

| Table-II. Follow up pain associated with fissure in-ano | | | | |
|---|---|---|---|---|
| **Week** | **Absent** | **Mild** | **Moderate** | **Severe** |
| 1st | 0% | 42.9% | 57.1% | 0% |
| 4th | 28.6% | 50.6% | 21.4% | 0% |
| 6-8th | 57.1% | 21.1% | 21.4% | 0% |
| 9-12th | 64.3% | 14.3%* | 7.1%* | 14.3%* |

| Table-III. Patient's compliance to GTN treatment | |
|---|---|
| Total patient reported | 306 (100%) |
| GTN treatment started | 276 (90.1%) |
| Defaulted to follow up | 114 (37.2%) |
| Desired GTN treatment | 246 (90.1%) |
| Refused / disliked GTN treatment | 42 (13.4%) |
| Demanded surgery after failure of topical treatment | 72 (23.5%) |

## DISCUSSION

Nitric oxide (NO) is a potent inhibitory neurotransmeter. Glyceryl trinitrate(GTN) is an organic nitrate that may absorb through skin/ mucosa and bind to nonadrenergic, noncholinergic nerve receptors, releasing nitric oxide, thus reducing tone and increasing blood circulation. Derangement of NO may result in sphincter spasm/ increase tone of internal anal sphincter or poor perfusion of ano-derm that leads to a vicious cycle in causing anal fissure[1,2,3,6]. Surgical interventions like anal stretch and sphincterotomy, have generally been aimed at overcoming this spasm[1,,2,6,11,15,21.22]. Major drawback of these modalities is uncontrolled tearing/damaging of the sphincter[14,15,21].

Preliminary results of small series suggest that topical application of nitro glycerin ointment is a new therapy that produces reversible reduction of sphincter pressure, allowing healing of the anal fissure.[8] Eighty three percent of anal fissure healed after two weeks of treatment with nitroglycerin ointment in a small pilot study[8]. A significant reduction in pain as assessed by linear analog pain score was observed within 5 minutes of application of the ointment. Lund [6] showed, topical glyceryl trinitrate ointment applied twice daily cured 18 of 21 patients. Mohammad[2] in a regional study found 75.5% healing of fissures and 8.1% recurrence rate. 24.4% of patients needed surgery. In this study a comparable healing rate is noted. Suhair[5] has much more comparable results in another regional study as 70% healing rate with 0.2% GTN, 60% headache and no response in 50% cases. Scholefield[9] in another study used different concentrations of GTN and showed healing rate of 46.9% for 0.1%, 40.4% for 0.2 % and 54.1 % for 0.4 % of GTN. Watson[22] used 2-8 % preparations of GTN and founded no advantage of higher concentrations but high incidence of headache. Local application of GTN reduces anal pressure and improves anodermal blood flow; this dual effect resulted in a healing rate up to 80 % at 7 weeks[5,7,11,15,16]. This study confirms the results of

other similar studies as healing of anal fissure in 57.1% cases with topical treatment was achieved. Various studies have shown healing rate up to 70% by GTN ointment[2,9,10,12,14]. Majority of studies has also shown increased anal blood flow[2,3,4,5,1012,17,19,22]. No major risk is involved in this modality as in the internal anal sphincterotomy, divsion may be more than was intended, especially in multiparous women, who may already have an unrecognized obstetric-related sphincter injury[14,15,21].

Sultan[21] have studied the drawback of injudicious surgical interventions and suggested that the anal canal ultrasound study is mandatory in multiparous women without continence problems in whom internal sphincterotomy is planned because, in the presence of an already existing sphincter defect, this procedure may result in severe fecal incontinence. Corby [14] showed that postpartum anal fissure is associated with reduced anal canal pressures; in this condition further surgical damage to the anal sphincter mechanism is a clear risk for incontinence. So the conservative methods are getting the popularity as there is no report of feacal incontinence during topical treatment[16].

Many patients experienced transient headache (range 19 % to 44 %) while using topical nitrates preparations, and an anal burring sensation has also been reported[2,5,9,10]. Reduction in pain was also significant but the headache was the major complaint by GTN ointment and it was not so severe which could lead to discontinuation of treatment /disturbance of job. In this study all patients experienced headache ranging from mild (71.4%) to moderate (28.6%) and 50% of them used analgesics for symptomatic relief $p<0.05$. Watson[22] reported a fissure-healing rate of 33 % with persistent or recurrent fissure in 44 % of patients and failure to complete treatment in 23% at 6 weeks. This study also showed similar results. As out of 276 patients 114 (27.6%) never reported for follow up. A better understanding and protocol to address the potential problems is essential so that short duration of treatment and side effects could be avoided[17]. In a similar local study, Zubairi[10] showed fissure healing in 66.7% in about 8 weeks, 72.2% headache, 5.6% flatus incontinence and recurrence rate 25% within six months of topical treatment. In this study we achieved comparable results in the local setup.

The advantage of using GTN is ensuring reduction in anal pressure for some time, which allows the fissure to heal thus eliminating the need for surgery, without any complications such as incontinence due to permanent sphincter damage. Topical treatment has a higher recurrence rate $p<0.005$ (highly significant). However patients who tend to avoid or are unfit for surgery, topical (GTN) is the treatment of choice. Symptomatic improvements were achieved. In conclusion the use of GTN appears to be a promising approach for treatment of anal fissure, particularly in patients at high risk of incontinence. More over patient can continue their job without any hospital stay. No severe adverse effect or permanent sphincter damage results from GTN application.

## CONCLUSION

In patients with chronic fissure in-ano, glyceryl trinitiate ointment is safe and effective modality that can be considered as first line of treatment especially in unfit patients or wishing to avoid/ delay surgery as it has no permanent side effects and is well tolerated.

Further larger randomized trial are needed for optimization its dose and efficacy in the local setup. Availability of commercial preparations may be more helpful in our country.

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