

Original Article

Therapeutic effectiveness of Glyceryl Trinitrate (GTN) in the Treatment of uncomplicated Chronic Anal Fissure (CAF)

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Abstract:

Objective: To determine the therapeutic effectiveness of Glyceryl trinitrate (GTN) in the treatment of uncomplicated chronic anal fissure

Materials and Methods: Prospective observational Study conducted in a private hospital in Dhaka City from Jan 2019 to Dec 2019. Forty eight patients of chronic anal fissure were included in this study. There were 28 (58.33%) females and 20 (41.66%) males with mean age of 37. Pain was documented using visual analogue scale. At presentation all patients (100%) perceived pain as severe pain on Visual Analogue Scale. Patients were started treatment with local application of Glyceryl Trinitrate (GTN) gel, twice daily and reassessed after 04 weeks and 08 weeks of treatment respectively. Pain and healing of fissure were documented.

Results: Significant pain relief was observed in 46% patient & fissure healing was observed in 31.25% patient. The commonest side effect of treatment was headache (26%).

Conclusion: Glyceryl trinitrate is very effective in the treatment of chronic anal fissure and is the drug of choice in conservative treatment of anal fissures and in patients with contraindications for surgery

Keywords: Chronic anal fissure, Glyceryl Trinitrate, Visual analogue scale

Introduction

Anal fissure is a painful tear in the distal anal canal, which usually involves only the epithelium but in the long term, involves the full thickness of the anal mucosa.¹ Fissures are caused by stretching of the anal mucosa beyond its capability. It affects nearly all age groups but particularly the adults.² Majority of the anal fissures occur in the posterior midline of the anal canal.³ The typical symptoms of anal fissure are anal pain during and after defecation associated with passage of bright red blood per rectum. The pain is often severe and may last for several minutes or hours.⁴ The most common cause is spasm of the internal anal sphincter muscle which results in impaired blood supply to the anal mucosa. The result is a non-healing ulcer, which may become infected by fecal bacteria. It has indurated edges on proctoscopy. Fissure base may reveal the presence of internal sphincter muscle fibres and sentinel skin tags may be present.⁵ Chronic anal fissure usually does not heal without some form of intervention. Treatment is directed at reduction of

internal sphincter tone and anal canal pressure. The gold standard of treatment of chronic anal fissure is lateral internal sphincterotomy resulting in healing rate of up to 98% of the patients.⁶ Among conservative modalities diet modification, stool softeners, laxatives and sitz bath are recommended. Analgesics and antibiotics are also used concomitantly. Second line therapy includes Glyceryl trinitrate (GTN) ointment, botulinum toxin, anal dilatation, calcium channel blockers, local anesthetics and steroids. GTN is emerging as first line treatment.⁷ It is a neurotransmitter mediating the relaxation of internal anal sphincter. Topical GTN results in healing of two thirds of chronic anal fissures.⁸ A regimen using 0.2% GTN ointment applied twice daily to anal canal for 8 weeks is the most commonly prescribed form of treatment.⁹ Headache is the major side effect of the treatment that is usually mild and transient.¹⁰ Due to our social traditions and taboos patients especially ladies do not readily accept the surgical treatment and ultimately suffer for long time. This study will help to

determine the efficacy of Glyceryl trinitrate in the treatment of chronic anal fissure as an alternative for surgical procedure if the patient is unwilling for surgery.

Materials and Methods

Prospective observational Study conducted in a private hospital in Dhaka City from Jan 2019 to Dec 2019. Forty eight patients of chronic anal fissure reporting with symptoms of pain in anal region during and after defecation and passage of bright red blood per rectum for more than one month duration and fulfilling the inclusion criteria i.e. 12-60 years of age from both sexes and diagnosed cases of chronic anal fissure. Patients having other anal pathologies and having history of migraine were excluded from the study. Patients underwent per rectal examination for confirmation of chronic anal fissure. Demographic information such as name, age, gender, and address were included in the study. Detailed history of the patient was taken followed by physical examination. Complications if any were registered. Patients were assessed for their current status. Pain was evaluated by visual analogue scale and data entered in a proforma. Patient were explained the treatment options available and the benefits of surgical procedure. Informed consent regarding unwillingness for surgery and willingness for conservative management using Glyceryl Trinitrate was taken. Prior permission was taken from hospital ethical committee. Patients were prescribed Glyceryl Trinitrate ointment, local application twice daily application for a period of two months. Patient were requested to visit again after one and two months of treatment respectively and assessed for pain and improvement in symptoms. Based upon the follow up assessment data was collected and entered into a proforma. Study variables were pain, bleeding episodes per rectum and complications.

Data Analysis

All the data was entered on SPSS version 15.0 for analysis. The descriptive variables were used to calculate frequencies and the data was presented as tables and figures.

Results

Forty eight patients were included in the study. There were 28(56.33%) females and 20 (41.66%) males shown on table 1. Age of the patients range between 16 to 59, mean ages was 37 years. The commonest age group affected was 20-30 years (41.66%) and least affected was 51-60 years (4.16%) table 2. All patients (100%) had severe pain on Visual Analogue Scale at presentation. After 04 weeks of Glyceryl Trinitrate application, 14

(29.16%) had mild pain, 30 (62.5%) had moderate pain and 4 (8.66%) had severe pain as shown in Table No 3. Re-evaluation of the patients after completing 08 weeks of treatment with GTN revealed that 22 (45.83%) patients had become pain free, 15 (31.25%) had mild pain, 9 (18.75%) had moderate pain and only 2 (4.16%) had severe pain as shown in Table No 4. Fissure healing was observed in 31.25% patient shown in table 5.

This showed that 46% patients had significant relief with GTN application for a period of 02 months. Fissure healing was observed in 50% patient. The common side effect of the treatment was headache which was effectively managed by Paracetamol.

Table-I: Sex of the population

Study population	Male	Female
48	20(41.66%)	28(58.33%)

The commonest age group affected was 20-30 years (41.66%) and least affected was 51-60 years (4.16%)

Table-II: Age of the study group

Age Distribution	N	%
<20	3	6.25%
21-30	20	41.66%
31-40	13	27.08%
41-50	10	20.83%
51-60	2	4.16%
Total	48	100%

Table-III: Pain on visual analogue scale after 4 weeks

Pain	N	%
Mild pain	14	29.16%
Moderate pain	30	62.5%
Severe pain	4	8.33%
Total	48	100%

Table-IV: Pain on visual analogue scale after 8 weeks

Pain	N	%
Pain free	22	45.83%
Mild	15	31.25%
Moderate	9	18.75%
Severe	2	4.16%
Total	48	100%

Table-V: Healing of anal fissure after 8 weeks

Healing	N	%
8 weeks	15	31.25%
Non healed	33	68.75%
Total	48	100%

Discussion

Lateral internal sphincterotomy (LIS) is considered the gold standard for the treatment of anal fissure. There is a wide variety of management options for conservative management but their effectiveness in the healing of anal fissures is variable. Healing may be temporary and recurrent fissures may need a change in treatment.¹¹ Conservative management include laxatives, diet modification, Sitz bath, anal dilatation, Botox injection. Drug options include Glyceryl Trinitrate ointment, nifedipine ointment, isosorbide dinitrate (ISDN), diltiazem, and clove oil. Nitric Oxide (NO) has been identified as the chemical messenger of the intrinsic non-adrenergic, noncholinergic pathway mediating relaxation of the internal anal sphincter. Exogenous NO donors such as GTN and ISDN also reduce anal pressure by relaxation of the internal anal sphincter.¹² Memon MR et al¹³ compared lateral internal sphincterotomy with local application of Glyceryl Trinitrate and found relief in 30% patients using Glyceryl Trinitrate but 100% relief was observed in patients undergoing LIS. Hashmat and Ishfaq¹⁴ in their study for comparison of surgical and pharmacological sphincterotomy found similar results with 100% cure in surgical group and 64.3% relief in chemical sphincterotomy group. Mustafa et al¹⁵ found relief in 70% of patients using Glyceryl Trinitrate and that oral nifedipine was equally effective to GTN in reducing anal pressure. Headache was the common side effect for GTN application. Sajid et al¹⁶ in their research compared Botox and diltiazem with Glyceryl Trinitrate in two different studies and found both to be equally effective except that GTN was more associated with headaches. Jawaid et al¹⁷ compared local application of diltiazem with Glyceryl Trinitrate and found them equally effective with 82.5% patients improving in GTN application but headache was the commonest side effect in GTN group. Scholefield et al¹⁸ in their study found that after eight weeks of treatment healing rates were 24% in the placebo group compared with 50% in the 0.1% GTN group, 36% in the 0.2% GTN, and 57% in the 0.4% GTN group. This study is comparable to this study in which we had a relief in pain in upto 46% of the patients included in the study.

Loder et al¹⁹ reported that resting pressure remained reduced for up to 9 hours after topical application of 0.2% GTN. In another study anal pressures had returned to pretreatment values in all 6 patients by 6 hours after application of topical 0.2% GTN. A fissure-healing rate of 43%, suggests that GTN should be used as firstline therapy for chronic anal fissures, LIS being reserved for fissures not responsive to GTN and recurrent fissures. Watson et al,²⁰ found that when anal fissures were treated with topical 0-2% glyceryl trinitrate on a twice daily regimen. An adequate pressure reduction (30%) was found in four of 13 patients. At six weeks the fissure healing rate was only 33%. Botulinum toxin injection is an effective alternative to surgery for the treatment of uncomplicated idiopathic anal fissure. Gui and coworkers²¹ used another technique, injecting botulin toxin into the internal anal sphincter on both lateral sides as well as posteriorly at the fissure site. One month after treatment anal resting pressure was reduced by 24%. After short-term follow up the healing rate was 84%. Glyceryl trinitrate and ISDN are much cheaper than botulinum. The only side effect reported so far is mild transient headache. Lund et al²² treated twenty one consecutive patients with chronic anal fissure. At six weeks the healing rate of fissures was 86%. For chronic anal fissures, the healing rate at 12 weeks of 50% in the study was lower than 86% in previous studies. No patients developed incontinence or soiling after GTN, which is more favorable than 7% transient incontinence in patients with treated with botulin toxin, or the reported incontinence rates of up to 30% in patients treated by lateral sphincterotomy. Headaches were reported by 60% of patients. Although surgery is the gold standard for the treatment of chronic anal fissure but in our socioeconomic conditions where there are financial constraints and patients specially females are reluctant to undergo surgery by male surgeons and patients having contraindications for surgery, Glyceryl Trinitrate use can be effective alternative treatment for such patients.

Conclusion

Conservative treatment with Glyceryl trinitrate (GTN) is an effective measure for the management of chronic anal fissure. This approach can be applied for uncomplicated chronic anal fissure and in patients who are unwilling for surgery or in whom surgical intervention is contraindicated. It is least invasive and has good patient compliance.

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J. Dhaka National Med. Coll. Hos. 2021; 27 (02): 26-29