

Comparison of Topical Glyceryl Trinitrate and Nifedipine in Management of Chronic Anal Fissure

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ABSTRACT

Objective: To compare the complete healing of chronic anal fissure by using 2% nifedipine paste and 0.5% glyceryl trinitrate ointment each applied locally for 6 weeks.

Study Design: Randomized Controlled Trial.

Place and Duration of Study: Surgical Unit-I, Pakistan Railway Hospital Rawalpindi spanning over a period of 06 months starting from March 2011 to August 2011.

Materials and Methods: Seventy six patients of chronic anal fissure were included in the study. Non-probability convenience sampling was used for the enrolment of patients. Patients were divided equally into two treatment groups A & B. Group 'A' was treated with topical 2% nifedipine paste and Group 'B' was treated with 0.5% glyceryl trinitrate ointment. Patients were asked to come for the follow up after six weeks to look for symptomatic improvement and healing rate.

Results: All 38 patients included in the study completed the follow up after 06 weeks of treatment in either group. Three patients from Group B experienced intractable headache and were managed by analgesics accordingly but they went on to complete the treatment. None of the patient in group A had any significant side effect causing any adjustment in the treatment. At the end of 06 weeks of treatment, 28 patients in Group A and 25 in Group B showed complete healing of anal fissure. The overall healing rate was 69.75 % (n=76). There was statistically no significant difference at the end of 06 weeks of treatment (p=0.454).

Conclusion: It is concluded that 2% nifedipine paste is as effective as 0.5% GTN ointment in terms of healing of chronic anal fissure.

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Key words: Chronic Anal fissure, GTN, Nifedipine.

Introduction

Anal fissure is one of the most common proctologic problems presenting with painful bleeding per rectum¹ estimated to be affecting 10% of the patients attending the colorectal clinics.² It is common condition affecting all age groups, but it is particularly seen in young and otherwise healthy adults usually in third and fourth decade.³

Chronic anal fissure is associated with persistent hypertonia of internal anal sphincter and high resting anal pressure.⁴ The manometric evidence has confirmed that the high resting anal pressure is caused by internal anal sphincter spasm and hypertonicity of sphincter as the fissure bed lies on the internal anal sphincter.⁵ All the current available treatment modalities of

anal fissure are aimed to focus on high resting anal pressure. The underlying principle of treating anal fissure is to reduce internal anal sphincter tone, thus reducing the resting anal pressure.⁶ This can be achieved both by pharmacological or surgical means.⁷

Surgical operations including anal dilatation and internal sphincterotomy are effective in lowering the resting anal pressure and decreasing the anal tone but carry a significant risk of impaired level of continence.⁸ Therefore, there has been a significant change during the last decade in the treatment of anal fissure with major emphasis on the conservative treatment modalities. These pharmacological methods are aimed at reversible relaxation of anal sphincter.⁹

Glyceryl trinitrate is regarded as the first line agent, which is widely used for chemical sphincterotomy.¹⁰ Although it has high

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healing rates but associated with major side effects like headache.¹¹ Calcium channel blockers, e.g. nifedipine, diltiazem are the other class of drugs which are used for chemical sphincterotomy with comparable healing rates with fewer side effects specially headache.¹²

There is no research conducted in our set up in which the efficacy of topical nifedipine for healing of chronic anal fissure is studied. Though nifedipine has been recommended as first line treatment in the management of chronic anal fissure in United Kingdom, it is neither dispensed nor used in tertiary care set ups due to lack of awareness and confidence about the drugs. Its cost is also comparable to GTN. This study is based on very limited available data on the better healing with topical nifedipine as compared to glyceryl trinitrate for chronic anal fissure. This would help in building the confidence of surgeons in adapting nifedipine, as a new treatment modality which can be used in tertiary care hospitals in local population.

Materials and Methods

It was Randomized Controlled Trail conducted at Surgical Unit-I of IIMC-T, Pakistan Railway Hospital Rawalpindi. The study was conducted on OPD basis over a period of 06 months starting from March to August 2011.

Sample size of 76 patients was calculated by using WHO sample size calculator. The sample was selected by using the consecutive (non-probability) sampling technique .First 76 adult patients, of both genders, having a history of anal pain, worsening with bowel movements, for duration more than 6 weeks, and on anal examination showing a longitudinal tear in the lining of distal anal canal below the dentate line, in the midline anteriorly or posteriorly and who gave consent to enter

the study were considered eligible for enrollment in the trial. Patients with acute anal fissure, fissures occurring in locations other than the midline posteriorly or anteriorly, and patients with TB, inflammatory bowel disease, anal carcinoma and recurrent anal fissure were not included in the study. Patients with multiple anal fissures and patients on other formulations of nitrates and calcium channel blockers for illness were also excluded from the study. After taking approval from hospital ethical committee and after explaining the purpose of the study, informed consent was obtained from the patients participating in the study. Patients were randomly assigned using the lottery method, to either topical nifedipine paste (2%) [Group A] or GTN ointment (0.5%) [Group B] .The assigned medication was applied locally both externally and internally about the size of a pea every 12 hours for six weeks by the patient. The outcome was noted as 'complete healing' or 'incomplete / no healing' at the end of 06 weeks based on inspection on digital rectal examination of the anal canal. First examination as well as follow up examination was done by consultants. Data collected from the patients was entered on the Performa. Data was analyzed using the Statistical Package for Social Sciences (SPSS version 16).

Results

From March 2011 to August 2011, 76 consecutive outpatients were enrolled on a convenient sampling bases; 38 patients received 2% Nifedipine paste (Group A), and 38 patients received GTN Ointment (Group B).Our study population was in age group of 11 to 60 years. Mean age of patients in our study was 31.36 years .The duration of symptoms varied from 06 to 40 weeks. The

maximum number of patients who fall in a specific duration were 14 (n=76) and that was 12 weeks followed by 11 patients in 08 weeks duration. Mean for duration of symptoms was 14.83. Standard deviation was 7.01.

The distribution of duration of symptoms is shown in the Figure 1.

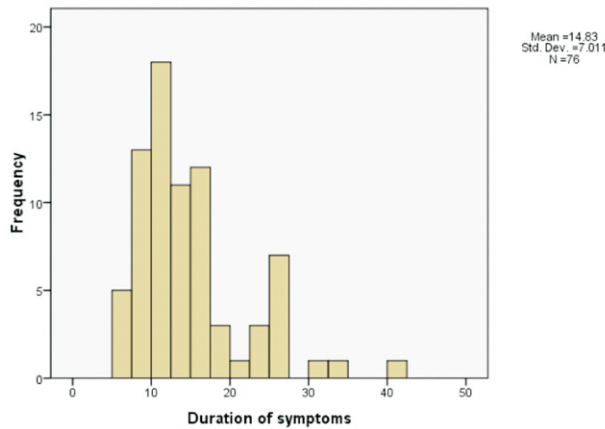


Figure 1: Duration of Symptoms in Weeks

In our study, 24 patients (31.6%) were male and 52 patients (68.4%) were female (n=76). There were 5 (6.67%) male and 33 (43.42%) female patients in the group A. On the other hand there were 19 (25%) male and 19 (25%) female patients in group B. The location of fissure is shown in the Table I

Table I: Position of Fissures(n=76)

Position	Frequency (n)	Percentage (%)
Anterior	19	25%
Posterior	57	75%
Anterior & Posterior	00	00%
Total	76	100%

All the patients in the study completed the follow up of 06 weeks of treatment in both group A and group B. Three patients (n=3) 3.94% from Group B experienced intractable headache and were managed by analgesics

accordingly but they went on to complete the treatment. None of the patient in group A

Table II: Outcome of Treatment(n=76)

Treatment Group	Complete Healing	Incomplete / No Healing	% of Healing
Nifedipine (Group A) N=38	28	10	73.68
GTN (GROUP B) N=38	25	13	65.79
TOTAL N=76	53	23	69.74

(P=0.454)

procedures. Incontinence is a major and irreversible complication. Topical GTN remains the most widely used non-surgical treatment for chronic anal fissure.¹³ GTN also remains the standard agent against which the other newer agents are compared in terms of efficacy and compliance.¹⁴ Aim of this study was to compare the efficacy of Nifedipine treatment against the glyceryl trinitrate in the management of chronic anal fissure.

According to literature, anal fissure is particularly seen in young and otherwise healthy individuals.^{15,16} Fissures have a predilection for the posterior midline (90 %) but may also be located in the anterior midline or lateral. The explanation for this

phenomenon is both anatomic and functional.^{17,18}

Calcium channel blockers such as nifedipine and diltiazem have been the focus of research in recent years regarding their role in fissure management. Cook et al. demonstrated the reduction of resting anal tone, inhibition of contraction of internal anal sphincter and the healing of anal fissure by using oral nifedipine.¹⁹ Our study showed that 73% of patients with chronic anal fissure could achieve complete healing by using topical nifedipine. This finding is lower than a comparable study conducted by Perrotti et al which showed the healing rates of over 95%.²⁰ They added topical lidocaine to nifedipine and compared it with the control. Perhaps the addition of local anesthetic to topical nifedipine has beneficial effect in lowering the anal tone.²¹ Ezri and Susmalliam showed better healing rates with topical nifedipine than GTN when used for anal fissure.²² There were more side effects in GTN group than the nifedipine group. Many controlled clinical trials have shown varied results in terms of fissure healing with the topical GTN (45-80%).²³ The major side effect of topical GTN therapy for anal fissure is that almost 40% of patients experienced headaches.²⁴ Masood et al demonstrated the healing of anal fissure in 82% of the patients with the use of topical GTN; however headache was experienced by 67% of the patients. Another known considerable drawback to GTN therapy is high recurrence rate.²⁵ Poor compliance with prescribed treatment often contributes to low outcome.

The healing showed in the GTN group in our study was 65% which is comparable to other studies in term of efficacy. Usman et al demonstrated the healing of anal fissure in 88% of patients after 06 weeks of topical

treatment with GTN. They compared topical GTN with internal anal sphincterotomy in chronic anal fissure. However, headache of variable intensity was reported in 40% of the patients.¹⁷

In a local study conducted at a tertiary care teaching hospital in Pakistan, in which the effect of topical GTN was studied in acute anal fissure, the healing rate of 68% was reported with GTN.¹⁷ In a prospective randomized trail which included 35 patients of anal fissure, Bacher et al demonstrated complete fissure healing in 80% of the patients after 04 weeks of topical GTN treatment against 40% of the controls.²⁶ This result was better as compared to many other studies in which healing was reported around 65-70% with GTN treatment.²⁷

Our study was unique in the way that a very few randomized trials available in the literature in which nifedipine was compared with the GTN in topical management of anal fissure. Ezri et al compared topical nifedipine and GTN in a randomized trial involving 52 patients. They found that the healing was higher with nifedipine (89% vs. 58%) with less frequent side effects (5% vs. 40%).²² Although the side effects profile was not made the part of work for which the study was conducted, but nevertheless, the number of headaches reported in our study were significantly lower in the nifedipine group than the GTN group. This had been shown in many previous studies.¹

We were unable to prove our hypothesis. Although nifedipine failed to show any statistically significant difference over GTN in terms of efficacy, still the rates of healing are comparable to other studies showing its effectiveness.

Conclusion

It is concluded that 2% nifedipine paste is as effective as 0.5% GTN ointment in terms of

efficacy in management of chronic anal fissure.

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