

# Topical Diltiazem is Superior to Topical Lignocaine in the Treatment of Chronic Anal Fissure: Results of A Prospective Comparative Study

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## ABSTRACT

**Introduction:** Fissure in ano is a troubling and painful condition that affects a great majority of the population the world over. Chronic anal fissures are associated with persistent hypertonia and spasm of the internal anal sphincter and they have conventionally been treated surgically. However, concerns have been raised about the risk of faecal incontinence after surgical sphincterotomy. In this study, we have explored topical 2% diltiazem as an effective and a safe alternative method to surgical treatment.

**Materials and methods:** In this prospective comparative study, 200 patients with chronic anal fissure from a single centre were included. They were randomly divided into the test group and the control group, with 100 patients in each group. The test group was instructed to apply 2% topical diltiazem ointment and control group was instructed to apply topical 2% Lignocaine twice daily for 6 consecutive weeks. They were asked to apply the medicine just inside the anal canal and 1cm around the anus circumferentially.

The assessment was done at the 2nd, 4th and the 6th week-ends for fissure healing, pain relief, bleeding control, control of

discharge/perianal itching and for the side effects of the medicines.

**Results:** Complete healing of the fissure was observed in 72% of the patients in the test group against 23% in the control group by the end of 6 weeks ( $P < 0.0001$ ). The pain relief was also good as the pain score in the test group dropped from 80 (mean) to 5 (mean) over the 6 weeks time. 80% of the test group cases experienced absent bleeding by the end of the 6th week as compared to 42% in the control group ( $P < 0.001$ ). 90% of the subjects in the test group reported a significant reduction in the discharge and the perianal pruritis as compared to 50 % in the control group ( $P < 0.0001$ ). 3 patients had a mild headache, while 10 patients experienced slight perianal pruritis. In the 1 year follow up, 4.28% subjects in the test group reported recurrence of the symptoms against 34.78% in the control group.

**Conclusion:** We conclude that 2% topical diltiazem is quite effective in the treatment of chronic fissure in ano.

**Statistical analysis used:** Chi square and P-value (SPSS software version 17).

**Key Words:** Fissure-in-ano, Sphincterotomy, Diltiazem

## INTRODUCTION

Anal Fissure (AF) is a linear tear in the anal canal, which is distal to the dentate line [1] and it causes considerable morbidity [2]. It is a common condition which affects all the age groups, but it is particularly common among young adults [1,3]. The aetiology is unclear. The main pathology appears to be persistent hypertonia and spasm of the internal anal sphincter that results in mucosal ischaemia [3, 4, 5].

Acute AF usually heals with simple measures such as stool softeners and dietary modifications. But chronic AF usually doesn't respond to such measures and a treatment is usually required, that is aimed at reducing the internal sphincter spasm with minimal complications [2]. Chronic AF has traditionally been treated by surgical sphincterotomy [1,6]. However, concerns have been raised about the risk of permanent anal incontinence [2,4]. Therefore, pharmacological means to treat chronic anal fissures have been explored [4]. The initial enthusiasm for chemical sphincterotomy with topical glyceryl trinitrate has waned because of side effects, particularly headache [6].

In a study which was conducted by Carapeti et al., [6,9] on fissure in ano by using topical diltiazem, fissure healing was noted in 67% of the cases [7, 8]. In another study, Knight et al., [1] reported fissure healing in 73% of the cases. In this study, topical 2% diltiazem ointment has been explored as an effective and a safe alternative method of chemical sphincterotomy.

## MATERIALS AND METHODS

This study was carried out at AJ Medical College Hospital, Mangalore from January 2009 to Dec 2011. 200 patients with chronic Anal Fissure (AF) were enrolled in this comparative, prospective clinical study which was cleared by the local ethical committee.

A written informed consent was obtained from the patients and they were given the choice to pull out from the study at any point if they wished to. The treatment protocol was considered to be dishonored if a patient didn't comply with the treatment as he/she was advised.

**The inclusion criteria were:** patients who were aged between  $\geq 18$  years and  $\leq 65$  years; the presence of chronic anal fissure for

more than 6 weeks that had failed to resolve with simple measures (stool softeners, a high fibre diet and a warm sitz bath); the physical examination had revealed fibrotic anal fissure with induration at the edges, an external skin tag, and exposure of the horizontal fibres of the internal anal sphincter on the floor.

The exclusion criteria were any history of reaction to topical agents and associated co-morbidity such as ischaemic heart disease, hypertension, diabetes mellitus, anal fistula, haemorrhoids, perianal abscess, inflammatory bowel disease, HIV-related fissure, tuberculosis ulcer, leukaemic ulcer, pregnancy and lactation.

The chosen patients were treated as outpatients. They underwent a detailed clinical examination which included a digital rectal and proctoscopic examination. Sigmoidoscopy and colonoscopy were performed as and when they were necessary.

They were randomized into the test group and the control group, with 100 patients in each group. They were subjected to the treatment with 2% topical diltiazem ointment for the test group and topical 2% lignocaine for the control group, twice daily for 6 consecutive weeks. The subjects were instructed to apply the medicine (about a size of pea) to just inside the anal canal and 1cm around the anus circumferentially by using the tip of their index fingers. The patients were encouraged to eat a high fibre diet and to use warm sitz baths.

They were called for follow up at the 2nd, 4th and 6th weekends during the course of the treatment and then bimonthly for a year. The parameters which were recorded at each visit were fissure healing, pain relief, control of the bleeding, control of the discharge and itching, any side effects and recurrence.

The healing of the fissures was assessed visually and the intensity of the pain was assessed from a visual analogue score. The healing was defined as a complete disappearance of the fissure on examination. Each patient was supplied with a pain score chart and he/she was educated on how to daily mark the level of pain on it. These charts were graded from 0 to 100 and they were marked at one end as 0- (no pain) and at the other end as 100- (worst pain). The disease was termed as recurrent if either the symptoms and/or the fissure reappeared 1 month after the 6 weeks course of the topical application.

The data was collected and analyzed statistically by using the SPSS, version 17 software. The p values were calculated by using the Chi-square test.

## RESULTS

In this study, the ages of the patients were fairly similar in both the groups [Table/Fig-1]. In both the groups, pain was the main presenting symptom, followed by bleeding per-rectum, anal discharge and pruritis [Table/ Fig-2].

54%-58% of the cases had associated constipation, which is a common cause of fissure. Posterior midline fissure was the commonest location and in most of the cases, there were external skin tags, indurated edges and exposed internal sphincter muscles on the floor.

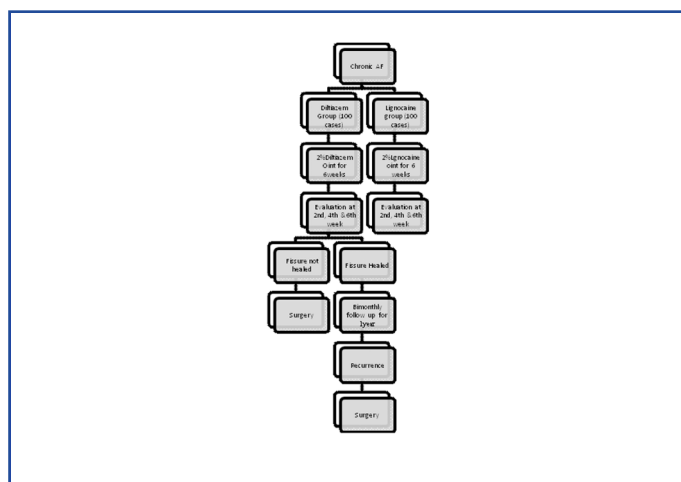
At the end of the 2nd, 4th and the 6th weeks, the test group and the control group were evaluated and compared. The parameters which were compared were fissure healing, pain response, bleeding response, discharge and peri-anal itching and side effects.

**Fissure healing:** Complete healing of the fissure occurred in 72% of the patients in the test group against 23% in the control group by the end of 6 weeks ( $P<0.0001$ , statistically highly significant) [Table/Fig-3 and 4].

The pain score in the test group dropped from 80 (mean) to 5 (mean) in 6 weeks time. A maximal effect was observed in the first 4 weeks [Table/Fig-5].

**Bleeding response:** The bleeding response was much better in the test group. Eighty percent of the test group cases experienced a significant fall in the bleeding by the end of the 6th weeks as compared to 42% in the control group ( $P<0.001$  statistically significant).

**Discharge and pruritis:** There was also a significant reduction in the discharge and the perianal pruritis as compared to those in the control group. In 90 of the 100 cases in the test group, the discharge and pruritis were absent, against 50 cases in the control group ( $P<0.0001$ , highly significant).



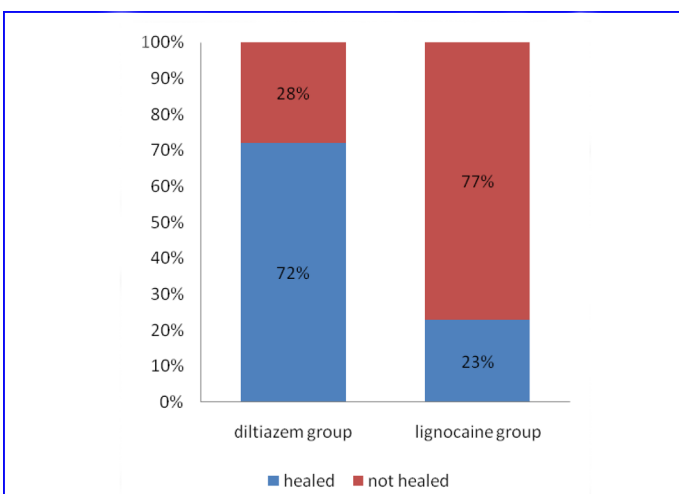
[Table/Fig-1]: Flow diagram from enrolment to final evaluation

Features/characteristic	Test group (N=100)	Control group (N=100)
Male	47	51
Female	53	49
Age in years (Range)	18-65	18-63
Age:Mean (Stand.deviation,SD)	38.97 (13.937)	40.17 (13.086)
Duration of symptoms (range)	6-9month	6-8months
Above 60		
<b>Symptoms:</b>		
Pain	97	94
Bleeding	86	83
Discharge/Itching	67	74
Constipation	58	54
<b>Local findings:</b>		
Posterior midline AF	76	70
Anterior midline AF	10	6
Anterior+ posterior AF	9	11
Multiple Fissures	5	13
Sentinel pile	85	82
Sphincter spasm	91	89

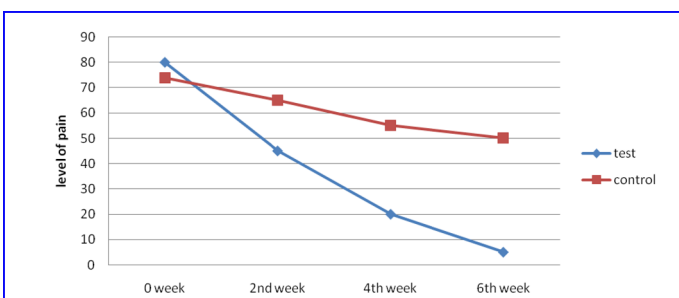
[Table/Fig-2]: Clinical details of the 200 cases studied have been shown

Fissure healing	Test group (N=100)	Control group (N=100)
At 2nd week end	0	0
At 4th week end	65	15
At 6th week end	72	23

[Table/Fig-3]: Fissure healing



[Table/Fig-4]: Fissure



[Table/Fig-5]: Pain Relief

Side effect	Diltiazem group (N=100)	Lignocaine group (N=100)
Head ache	3	0
Perianal itching	10	4

[Table/Fig-6]: Adverse effects of medicine

**Adverse effects of the medicines:**

Mild headache was experienced by 3% of the patients in the test group, while none of the cases in the control group reported about it (P<0.0001). All of them responded to paracetamol. Perianal itching was another side effect which was reported by 10% of the cases from the test group as compared to 4% in the control group (P<0.0001) [Table/Fig-6]. The pruritis was mild and it didn't require any treatment.

All the patients in the test and the control groups completed the full 6 weeks course of the treatment. However, 7 of the 72 fissure healers in the test (diltiazem) group and two among the 23 fissure healers in the control group didn't turn up for the follow up, while the rest completed the full 1 year follow up.

**Recurrences:**

Recurrence was observed in 3 of the 65 (4.61%) cases in the test group and in 8 out of the 21 (38%) cases in the control group.

**DISCUSSION**

Anal fissure is one of the common causes of severe anal pain and it causes considerable morbidity [1-9]. The posterior midline is the commonest site, followed by the anterior midline, particularly in females [3]. Fissure is often initiated by constipation [9]. In females, it frequently occurs during pregnancy and following childbirth [9]. There is an associated spasm of the underlying internal sphincter muscle which results in severe pain and impaired fissure healing.

An acute fissure (less than a month's duration) usually heals spontaneously or with simple measures like a high fibre diet, adequate water intake, and warm sitz baths [1,9]. The chronic anal fissures are not usually amicable to the aforementioned simple conservative measures [1]. A number of therapies have been described-non-operative and operative. The non-operative methods include the injection of botulin toxin to the fissure, oral nifedipine, the topical application of Glyceril Trinitrate (GTN) and topical diltiazem ointment [9].

Topical GTN is the most extensively tried non-surgical treatment for chronic anal fissure [1,2,10]. The topical GTN ointment or a GTN patch which is applied to the anal verge results in the healing of approximately two-thirds of the chronic anal fissures [11,12]. But, side effects such as headache and dizziness are common with nitrates, which may limit their application and reduce the patient compliance [12]. Besides, the tolerance to nitrates is a well recognized phenomenon [12]. Another drawback of the GTN therapy is the high recurrence rate which is associated with it [2].

Nifedipine and diltiazem are calcium channel blockers which act by blocking the slow L-type calcium channels in the smooth muscle, thus causing relaxation [1]. A number of studies have reported fissure healing in 60% to 75% of the cases with topical diltiazem [6,7,13,14]. Carapeti et al., [6,9] and Knight et al., [1] observed a fissure healing rate of 67% and 73% respectively in their studies.

They have also been tried successfully in the treatment of chronic AF that has failed to respond to GTN [8,15]. The topical diltiazem cream causes less headache and fewer side effects than the GTN ointment, without a significant difference in the healing rates between the two agents [6,16]. Also, the recurrence rate has been known to be lower with topical diltiazem [16,17-19].

**CONCLUSION**

In our study, fissure healing was found in 72% of the cases who received topical diltiazem. The pain relief was satisfactory in a majority of the cases. Headache and perianal itching were the two common side effects which were reported by some of our subjects. However, they were mild and tolerable.

One of the drawbacks which were observed was the patient compliance, as the duration of the treatment was quite long i.e. 6 weeks.

We conclude that 2% topical diltiazem is quite effective in the treatment of chronic fissure in ano. It may be considered as a first line treatment for chronic fissure in ano.

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