

## A Comparative Study To Evaluate The Effectiveness And Complications Associated With Topical Diltiazem Versus Open Partial Lateral Internal Anal Sphincterotomy For Chronic Anal Fissure.

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### Abstract:

**Background:** Anal fissure is a one of the most common and painful benign anorectal disease and its clinical management is still controversial despite several systematic reviews. Chronic anal fissure is defined by a history of symptoms present for more than 2 months' duration and with a triad of external skin tags, namely, a hypertrophied anal papilla, an ulcer with rolled edges, and a base exposing the internal sphincter. Because complications such as incontinence are associated with surgical treatment, chemical sphincterotomy is currently favored.

**Objectives:** The objective of this study is to compare the difference in outcome between open partial lateral internal sphincterotomy and application of topical 2% diltiazem ointment for the treatment of chronic anal fissure.

**Methods:** This was a quasi-experimental study carried out between August, 2016 and July, 2017 in the Upgraded Department of Surgery, Darbhanga Medical College & Hospital, Laheriasarai, Darbhanga, Bihar. Sixty consecutive cases with a clinical diagnosis of chronic anal fissure were recruited in the study. All recruited patients met the study inclusion criteria and were randomly assigned to one of the two groups. Group A was managed conservatively using topical 2% diltiazem ointment, whereas Group B underwent open partial lateral internal sphincterotomy. Both groups were followed up at 1 week, 2 weeks, 4 weeks, and 6 weeks after the treatment.

**Results:** All the patients complained of pain. A total of 43 (71.7%) patients had pain with constipation, whereas 31 (51.7%) patients had bleeding per rectum. Upon clinically examining the anal area, tenderness was elicited in all 60 (100%) patients. Group A included 30 (11 females and 19 males) cases treated with topical 2% diltiazem ointment and Group B included 30 (11 females and 19 males) cases who underwent open partial lateral internal sphincterotomy.

In Group A, only 15 patients with fissures were successfully treated (50%). By contrast, 28 (93%) patients with fissures in Group B were successfully treated, and only two (7%) remained uncured. These two patients (6.6%) in Group B suffered from incontinence due to flatus and feces as a complication of the procedure.

**Conclusion:** This quasi-experimental study demonstrates that open partial lateral internal sphincterotomy is superior to topical 2% diltiazem application in the treatment of chronic anal fissure, with good symptomatic relief, high rate of healing, fewer side effects, and a very low rate of early continence disturbances.

**Keywords:** Chronic anal fissure, open partial lateral internal sphincterotomy, calcium channel blocker, topical diltiazem.

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## **I. Introduction**

Anal fissure is one of the most common lesions to be considered in the differential diagnosis of anal pain. The commonly accepted definition of anal fissure is "A linear ulcer of the anoderm, distal to the dentate line, generally located in the posterior midline"<sup>1-4</sup>. It typically causes episodic pain that occurs during defecation and persists for 1 to 2 hours afterward.<sup>5</sup>

The most consistent finding in typical fissures is spasm of the internal anal sphincter, which is so severe that the pain caused by the fissure is thought to be due to ischemia of the sphincter.<sup>6</sup> Morbidity from operative procedures, mainly incontinence, was once thought to be extremely rare<sup>7</sup>, but has been substantial in some recent reports.<sup>8</sup>

The choice of treatment remains difficult for the following reasons. Although surgery is highly efficacious and successful in treating the fissure in more than 90% of patients, in a systematic review of randomized surgical trials, the overall risk of incontinence was approximately 10%.<sup>9</sup> This was mostly due to flatus incontinence, and there are no reports delineating the duration of this problem.

Regarding medical treatment, in a similar systematic review combining all analyses in which a placebo was used as the comparison group,<sup>10</sup> the healing rate in the placebo group was found to be 35%. This was a level of response that was fairly uniform across studies (standard deviation: 12%). The medications being tested in the meta-analysis (diltiazem ointment, botulinum toxin injection, and nitroglycerine ointment) must have their efficacy viewed in the context of this placebo effect and also in the context of a cure rate for surgery that often exceeds 95%.<sup>9</sup> In the combined analyses, diltiazem ointment was found to have a healing rate of about 55%. In addition, with diltiazem ointment, the most investigated medical treatment, headache was common, occurring in almost 40% of patients in the combined analyses and often severe enough to stop treatment.<sup>10</sup>

Therefore, it would be advantageous if the risk of incontinence could be reduced after the surgery or if the success rate of various other medical treatments is increased to that reported after a surgery, but with less risk of headache. The risk of using such treatments is not high, as patients mainly only experience headache while using the diltiazem ointment, without any apparent adverse effect in the long term. Medical treatments can therefore be used in individuals wanting to avoid surgical treatment, and surgery can be reserved for treatment failures in adults with chronic typical fissure. We wanted to study scientifically whether the outcome of surgical management among these patients is better than conservative (medical) approach.

## **II. Patients And Methods**

This study was carried out between August, 2016 and July, 2017 in the Upgraded Department of Surgery, Darbhanga Medical College & Hospital, Laheriasarai, Darbhanga, Bihar (study duration: 1 year). A total of 60 consecutive cases with clinical diagnosis of chronic anal fissure were recruited. All the participants fulfilled the inclusion criteria, which were evaluated using convenient nonprobability sampling.

### **2.1. Sample size:**

The 60 patients with chronic anal fissure were divided into two groups, namely, Group A [i.e., topical application of 2% diltiazem ointment (n=30 cases)] and Group B [i.e., open partial lateral internal sphincterotomy (n=30 cases)].

### **2.2. Inclusion criteria:**

The study included patients with chronic anal fissure, either gender, and age between 20 years and 60 years.

### **2.3. Exclusion criteria:**

The exclusion criteria for the study were as follows: pregnant ladies, patients with inflammatory bowel disease & hypothyroidism, patients with recurrent anal fissure, patients with hemorrhoids, and those not willing for treatment.

### **2.4. Ethical issues:**

All the patients were examined and investigated only after obtaining informed consent. Adequate privacy and presence of chaperone were ensured. Those patients who were treated surgically signed a written consent form.

### **2.5. Data collection procedure:**

Sixty consecutive cases of anal fissure diagnosed clinically with digital examination were registered to participate in the study. A written informed consent was obtained from all the patients after they were briefed about the procedures of fissure management. All patients met the inclusion criteria and were randomly assigned to one of the two groups. The demographic data including name, age, gender, and address were recorded. A topical anesthetic ointment (lignocaine gel) was routinely applied 5 to 10 minutes prior to the patients undergoing digital examination. The patients who were managed conservatively (Group A) were supplied with

2% diltiazem ointment, and were advised to rub the paste every 8 hours with a gloved finger. The treatment was carried out for 6 weeks. Patients were followed up at 1 week, 2 weeks, 4 weeks, and 6 weeks after the treatment with special consideration to pain relief, healing of fissure, and side effects of treatment. The pain severity was recorded as mild, moderate, and severe. Analgesics, sitz bath, and laxatives were standard options to treat pain. The patient is considered to be successfully healed when the breach in mucosa was completely treated and the patient had not experienced pain during defecation. Group B underwent open partial lateral internal sphincterotomy and the patients were followed up at 1 week, 2 weeks, 4 weeks, and 6 weeks after the treatment.

## **2.6. Data analysis:**

All the information collected was entered in a designed performa, as shown in [Appendix 1](#), and analyzed. The variables analyzed were demographic variables (name, age, gender), severity of pain, constipation, and bleeding per rectum. Quantitative data such as age were presented as mean and standard deviation, whereas qualitative data such as gender and pain were presented as frequency distribution table. A comparison of the outcomes between the two procedures was made by Chi-square test, as the variables were qualitative in nature. A p value <0.05 was considered significant.

## **III. Results**

A total of 60 patients with clinical diagnosis of chronic anal fissure were included in this study. In Group A, the minimum age of the participants was 20 years and the maximum age was 58 years (mean age:  $38.20 \pm 12.3$  years). In Group B, the minimum age of the participants was 21 years and the maximum age of the participants was 58 years (mean age:  $38.4 \pm 13.03$  years). A total of 22 (36.6%) participants were female (11 in each group) and 38 (63.3%) were male (19 in each group).

All the 60 patients complained of pain (100%). However, the severity of pain varied. A total of 13 patients recorded pain as moderate (21.7%), whereas 47 (78.3%) patients recorded it as severe. Constipation was found in 43 (71.7%) cases and 31 (51.7%) individuals presented with bleeding per rectum.

Taking the site of the fissure into account, 49 (81.6%) patients presented with posterior anal fissure, whereas 11 patients (18.4%) presented with anterior anal fissure. Most patients with anterior anal fissure were females. Upon clinically examining the anal area, tenderness was elicited in all the 60 (100%) patients.

No pain was experienced by 17 patients after topical 2% diltiazem application, but one patient reported persistent pain after lateral internal sphincterotomy.

The bleeding was taken into account at 2 weeks' interval after the completion of treatment. In Group A, which included patients treated with 2% diltiazem, 17 patients

presented with bleeding at 2 weeks' follow-up. By contrast, in Group B, which included patients treated with lateral internal sphincterotomy, only two (6%) patients presented with bleeding at 2 weeks' follow-up.

No headache and perianal itches was reported by 10 (33%) patients in Group A during the treatment with topical diltiazem. No incontinence was reported by patients in both Group A and Group B; however, two (6.6%) patients developed incontinence due to flatus and feces as a complication of procedure.

In Group A, the anal fissure successfully healed in 15 (50%) patients, whereas in Group B, the anal fissure successfully healed in 28 (93%) patients after lateral internal sphincterotomy ([Table 1](#)).

All the patients were followed up until 6 weeks after the completion of treatment and 15 (50%) patients in Group A were not completely cured from the fissure, which reflects the failure of treatment using topical 2% diltiazem. In Group B, however, 28 (93%) patients were completely cured at 6 weeks' follow-up, which proves the success of lateral internal sphincterotomy as a treatment of choice for anal fissures.

## **IV. Discussion**

Historically, the most common approach for relieving the pain associated with spasm of chronic adult anal fissure is surgical, yet no placebo-controlled surgical trials have been carried out. Surgery is usually associated with high costs, increased recovery time, and risk of incontinence. Therefore, by the late 1990s when alternatives to surgery were sought rather than turning back to older treatments, such as lubricants and numbing agents, newer medications were investigated-in each case, a medication that was known to relax muscle spasm was used. Such medications included nitroglycerin ointment, injection of botulinum toxin, and calcium channel blockers, which are either given as tablets or applied topically.

The encouraging results of early clinical trials of 2% diltiazem suggested that it might find a role in the treatment of anal fissures. Most studies tried to establish the role of 2% diltiazem, a non dihydropyridine calcium channel blocker, which is an important internal anal sphincter relaxant. In these previous studies, anal manometry and assessment of squeeze pressure were the methods used to evaluate the effectiveness of 2% diltiazem. Manometry showed 2% reduction in maximum resting pressure and squeeze pressure fell by 11%.

This is parallel to criteria used in this study, wherein place of objective evidence and improvement in pain and healing of fissure were used to assess treatment efficacy.

**Table 1: Results after 6 weeks of treatment.**

	2% diltiazem (n=30)	Open lateral internal sphincterotomy (n=30)	p value	
No pain after the treatment		17	29	0.0001
No bleeding after the treatment		17	28	0.001
No headache with the treatment		10	30	0.0001
No perianal itches with treatment		10	30	0.0001
No incontinence after the treatment		30	28	>0.5
Fissures healed after 6 weeks		15	28	0.0001

Gorfine<sup>11</sup> adopted a similar methodology in 1995 that used clinical evidence to assess the efficiency of treatment. A visual analog scale for pain adopted from a previous study proved to be effective yet simple to evaluate the subjective improvement.<sup>12</sup>

It was seen that the pain score fell more progressively and permanently from 10 to 2 with surgery as compared with 10 to 4 for topical ointment, but after 6 weeks, the score again rose to 6 or 7 in patients treated with topical ointment. Prior to widely adopting this form of treatment, a comparison with the current standard open lateral internal sphincterotomy must be made.

In this study, using a 0.5 ml dose of 2% diltiazem, we have observed healing of the fissure in 50% of patients after 6 weeks, which is comparable with the results of Lund and

Scholefield<sup>13</sup> and other studies.<sup>6,11,14</sup> Although 2% diltiazem was less effective in healing the fissures, it was quite effective in reducing the symptoms and minimizing the pain when used. Once 2% diltiazem was discontinued, pain recurred in a few patients, following which almost 30% of patients required surgery in this group after 6 weeks.

The fissure healing rate with open partial lateral internal anal sphincterotomy was 93.3%, whereas that for 2% diltiazem was 50% (p=0.0001), which is comparable to previous studies, in which the healing rate with open partial lateral anal sphincterotomy was reported to be 94 to 100%.<sup>15-17</sup>

Richard et al<sup>18</sup> concluded that surgical sphincterotomy improved healing rate at 6 weeks (89% vs. 29%) and reduced the further requirement for surgery (3% vs. 89%) in his trial of 82 patients.

With regard to symptoms, pain persisted in 13 (43%) patients treated with 2% diltiazem, whereas only one patient (3.3%) treated surgically complained of persistent pain. Similarly, bleeding per rectum persisted in 13 patients (42%) who applied diltiazem ointment. By contrast, bleeding per rectum persisted in only two patients (6%) among those treated surgically.

Incontinence as a complication of the procedure was reported in only two (6.6%) patients treated surgically, which is a result similar to that reported in previous studies.<sup>19,20</sup> One might argue that a more objective measure such as anal manometry should have been performed to assess anal sphincter status; however, we felt that the clinical symptom status was more relevant. Although this study suggests that continence is not adversely affected in the short term, further prospective evaluation with a comparison of control groups is needed to determine the long-term effect.

Different studies showed high rate of headache with 2% diltiazem, but in our study it was 67%, which was controlled by simple analgesics.<sup>19-20</sup> A mean healing period of 4 weeks was observed in Group B, whereas for Group A it was 6 weeks, which was similar to that achieved by Coher A,<sup>15</sup> Gorfine,<sup>11</sup> and Lund and Scholefield.<sup>13</sup>

**V. Limitations**

Only 6 weeks follow up period after the treatment, which was not enough to reflect any long-term results or recurrence, subjective definitions of itching and lack of anorectal manometry examinations and data regarding the effect of each treatment on anal sphincter pressure at rest and contraction are the key limitations of this study.

**VI. Conclusion**

This quasi-experimental study demonstrates that open partial lateral internal anal sphincterotomy is superior to the topical application of 2% diltiazem ointment in the treatment of anal fissure, with the advantages of good symptomatic relief, high rate of healing, fewer side effects, and a very low rate of early continence disturbances.

**Appendix 1**

**Performa**

Case no.\_\_\_\_ Hospital Reg no.\_\_\_\_ Group\_\_\_\_ Date\_\_\_\_  
Name: \_\_\_\_\_ Age: \_\_\_\_\_ Sex: \_\_\_\_\_  
Occupation: \_\_\_\_\_  
Address: \_\_\_\_\_

**Complaints**

Pain: \_\_\_\_\_ Severity: \_\_\_\_\_ Duration: \_\_\_\_\_  
Constipation: \_\_\_\_\_  
Bleeding per rectum: \_\_\_\_\_  
Soiling on cloth: \_\_\_\_\_

**Examination**

Location of fissure: \_\_\_\_\_ Size/extent: \_\_\_\_\_  
Associated pathology: \_\_\_\_\_ Tenderness: \_\_\_\_

**Investigation**

Routine  
Complete blood: \_\_\_\_\_  
Urine: \_\_\_\_\_  
X-ray (chest) PA view: \_\_\_\_\_  
ECG: \_\_\_\_\_

**Outcome of treatment**

Persistence of pain: \_\_\_\_\_  
Persistence of bleeding at 2 weeks: \_\_\_\_\_  
Incontinence to flatus: \_\_\_\_\_  
Soiling of under cloth: \_\_\_\_\_  
Recurrence of fissure: \_\_\_\_\_  
Headache/dizziness with 2% diltiazem application \_\_\_\_\_

**Overall results**

Fissure healed or not at 6 weeks: \_\_\_\_\_  
Change of treatment due to non healing at 6 weeks: \_\_\_\_\_  
Recurrence of fissure: \_\_\_\_\_  
Recurrence requiring surgery: \_\_\_\_\_  
Recurrence treated with application of 2% diltiazem paste: \_\_\_\_

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