

# Comparison of Effectiveness of Topical Versus Oral Nifedipine for Treatment of Chronic Anal Fissure

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## ABSTRACT

**Objective:** To compare the effectiveness of topical and oral Nifedipine in the treatment of chronic anal fissure.

**Patients and Methods:** In this randomized control trial total of 124 patients with chronic anal fissure (CAF) were selected through OPD and divided randomly into two equal groups. In Group A the topical Nifedipine (2%) was applied, while in Group B the oral Nifedipine 10mg TDS was used. Both groups were compared in terms of pain and healing measured one month after starting treatment.

**Results:** Mean age of the patients was  $38.81 \pm 11.81$  years. In both groups there was statistically significant difference for the age but no difference was found regarding gender and baseline visual analogue scale. Group A had better healing rate and pain relieve as compared to Group B. There was no difference between groups regarding the effectiveness of treatment.

**Conclusion:** The topical Nifedipine has better healing effects as compared to the oral Nifedipine. The oral form is better in relieving pain after one month of treatment. There was no difference between oral and topical form in terms of overall effectiveness.

**Key words:** Fissure in Ano, Nifedipine, Pain.

### Author's Contribution

<sup>1,2</sup> Conception, synthesis, planning of research and manuscript writing

Interpretation and discussion

<sup>3,4</sup> Data analysis, interpretation and manuscript writing, <sup>5</sup> Active participation in data collection.

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## Introduction

Anal fissure is one of the most common and painful proctologic disease in general surgery. It occurs mostly between the second and fourth decades of life with a lifetime incidence of 11%.<sup>1</sup> Frequency of anal fissure is approximately equal between men and women.<sup>1</sup> Up to 11% of women develop this condition after childbirth. Approximately 90% of anal fissures in both men and women are located posteriorly in the midline. Anterior fissures occur in 10% of patients and is more common in

women.<sup>2</sup> Less than 1% of fissures are located off a midline position or is multiple in number.<sup>3</sup> Raised resting sphincter pressure leads to relative ischemia especially in posterior midline ulceration, which results in persistence of internal sphincter hypertonia.<sup>4</sup> Lateral internal sphincterotomy (LIS) is a surgical treatment, considered as the 'gold standard' therapy for chronic anal fissure<sup>5</sup> and less than 10% long term recurrence<sup>6</sup> but associated with postoperative incontinence in 30% (or even more)

patients which can become permanent.<sup>7</sup> Most previous national and international researches were based on the efficacy of topical agents in anal fissure management. Topical CCBs (Calcium Channel Blockers) have been shown to be better than both lignocaine ointment and hydrocortisone cream.<sup>7</sup> Usage of oral Nifedipine was suggested in some studies for anal fissure therapy.<sup>8</sup> Topical Nifedipine is better in terms of wound healing for treatment of anal fissure as compared to oral Nifedipine whereas oral therapy is better in terms of pain reduction.<sup>4</sup> Since no national trial was found comparing the two forms of Nifedipine and international data is conflicting in support of both forms of treatment. This trial was conducted to compare topical Nifedipine with oral Nifedipine in chronic anal fissure in terms of healing and pain relief after 1 month in our population so that better treatment option could be adopted which would help in decreasing morbidity and hospital visits.

### Patients and Methods

This randomized control trial was conducted at Department of Surgery PAEC General Hospital Islamabad. Duration of the study was 6 months (20 December 2015 to 20 June 2016). Total calculated sample size was 124 patients, 62 in each group. Sample size was calculated through WHO sample size calculator by using 5% level of significance, 80% power of test, 95% confidence level, 49.5% anticipated population mean pain score (P1) and 73.3% anticipated target population mean pain score (P2).<sup>4</sup> Both male and female patients, who presented with anal fissure having age range between 18 to 60 years and baseline pain score  $\geq 4$  on VAS were included in study. Patients with history of sexually transmitted disease (STDs), tuberculosis, irritable bowel disease or anal cancer, presence of medical related problems such as diabetes mellitus, migraine and cardiovascular diseases, pregnancy and lactation, hypersensitivity to nifedipine or calcium channel blockers and cirrhosis were excluded from the study.

After taking the ethical approval, all the patients fulfilling the selection criteria were included in the study. Informed written consent was taken and patients were randomly divided into two equal groups, A & B. Randomization was done through lottery method. In group A, patients were prescribed to apply topical nifedipine cream (2%) at the

anal margin 8 hourly. Patients in the second group were given 10 mg oral nifedipine TDS, for four weeks. All

patients were advised to increase their intake of fiber and usage of sitz bath for 10-15 minutes, 2-3 times daily. On the first visit and follow-up visit at 4th week, wound healing and pain relief were recorded on Performa. For pain measurement, a visual analogue scale was devised between 0 and 10. Patients were asked to give 0 point to no pain and 10 for the worst pain they ever experienced. Wound healing was assessed by naked eye examination of wound for the development of granulation tissue and re-epitheliazation of the wound. Overall effectiveness was assessed by patient feedback in terms of no pain while passing stool and on local inspection of wound healing on follow up.

All the data was entered and analyzed using statistical package for social sciences (SPSS version 17). Means and standard deviations were presented for numerical values i.e., age and visual analogue scores for pain. Frequency and percentages were presented for categorical data like gender and wound healing. To compare the proportions of the patients with effectiveness in both the groups, Chi square test was applied.  $p < 0.05$  was considered statistically significant.

### Results

Out of 124 patients, 60(48.4%) were male and 64 (51.6%) were female patients. Mean age of the patients was  $38.81 \pm 11.815$  years. The baseline pain score was  $5.97 \pm 1.41$  at the start of the treatment. When the baseline pain scores were compared between groups at start of the treatment, then there was no statistically significant difference between groups (Table 1). At the end of one month, pain was relieved (VAS  $\leq 2$ ) in 59 patients (47.6%). Healing was observed in 64 patients (51.6%). Overall, the treatment was effective in 28 patients

**Table 1: Baseline VAS score comparison between groups (n=124)**

Group	Pain score (mean $\pm$ SD)	p-value
A	6.02 $\pm$ 1.38	0.704
B	5.92 $\pm$ 1.44	

(22.6%). Both the groups were compared regarding the pain and healing at the end of one month. Regarding pain and healing, Group A had significantly better effects as compared to Group B. There was no significant difference between groups when the effectiveness of the treatment was compared (Table 2).

**Table 2: Comparison of outcomes between groups at end of month (n=124)**

	Groups	Status		p-value
		Yes N (%)	No N (%)	
Healing	Group A	40(64.5)	22(35.5)	0.004
	Group B	24(38.7)	38(61.3)	
Pain	Group A	36(58.1)	26(41.9)	0.019
	Group B	23(37.1)	39(62.9)	
Overall Effectiveness (pain relief + healing)	Group A	13(21)	49(79)	0.668
	Group B	15(24.2)	47(75.8)	

### Discussion

Chronic anal fissure (CAF) is a condition when the anal fissure is there for more than six weeks at anoderm. Most of the time acute stage is usually treated with conservative management but the chronic condition usually needs surgical intervention. Various drugs used have variable results in terms of symptoms and healing rates.<sup>9</sup> Glyceryl trinitrate (GTN) is smooth muscle relaxant and vasodilator and it is more effective when it is used topically for treatment of CAF.<sup>10,11</sup> CCBs are good alternative for those who did not tolerate the GTN. CCBs can be used topically as well as orally. The CCBs have some side effects like headache, dizziness, itching and burning at the site of application.<sup>12,13</sup>

The local injection of the botox toxin is effective in short term for the treatment of CAF.<sup>14</sup> Cook, T. A., et al showed that the resting anal pressure is reduced by taking the Nifedipine orally and it results in the quick healing of CAF.<sup>15</sup> Similar results were shown by the other studies later on.<sup>16,17</sup> Ho, K. S. and Y. H compared the LIS and oral Nifedipine and the results showed that LIS was significantly more effective than oral Nifedipine in providing pain relief (P = 0.004) and better patient satisfaction (P = 0.020) at 4 weeks.<sup>18</sup> Another study

showed that the LIS and topical form of Nifedipine showed similar results in terms of healing and pain relief.<sup>19</sup> Golfam, F., et al. concluded that topical Nifedipine has a superior role for anal fissure treatment with higher healing rate and lower side effects as compared to oral one.<sup>4</sup>

### Conclusion

The topical Nifedipine is more effective in relieving the pain and healing as compared to oral form in CAF. Multicenter research work on large scale is recommended to evaluate the oral and topical forms of Nifedipine for the treatment of CAF.

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