

# Topical Combination of Nifedipine with Lidocaine for Anal Fissure Treatment

Rasha Kadim Albayati<sup>1</sup>, Adel Musa Al-Rekabi<sup>2</sup>, Nahedh R. Alammari<sup>2</sup>, Hayder Adnan Fawzi<sup>3</sup>

<sup>1</sup>Department of Surgery, Al-Diwaniyah Teaching Hospital, Al-Diwaniyah, Iraq, <sup>2</sup>Department of Surgery, College of Medicine, University of Al-Qadisiyah, Al-Diwaniyah, Iraq, <sup>3</sup>Clinical Pharmacy Departments, Baghdad Medical City Hospitals Campus

## ABSTRACT

**Background:** A fissure consist of crack or tear in the vertical axis of the anal canal between the anal verge and the dentate line. Anal fissure is treated by two ways either medical or surgical treatment or both.

**Objective:** evaluate the healing response of topical application of nifedipine with lidocaine in acute and chronic anal fissure

**Material and method:** A prospective study of one hundred patients presented with anal fissure to outpatient surgical clinic in Al-Diwaniyah teaching hospital, the patients divided into two groups, 40 patients (15 males and 25 females) with acute anal fissure, and 60 patients (25 males and 35 females) with chronic anal fissure.

**Results:** There was no statistically significant difference in the healing rate between acute and chronic lesion, however the rate of healed lesion in acute setting is higher than that of chronic setting (80% vs. 56%)

**Conclusion:** Topical application nifedipine and lidocaine effective in treating acute anal fissures with the healing response of 85%, and prevent evolution of acute anal fissures to chronic anal fissure.

**Keywords:** acute, chronic, anal fissure, Medical treatment.

## INTRODUCTION

Anal fissure is the most common cause of severe anal pain and bleeding<sup>1</sup>. Anal fissure is an elongated ulcer in anoderm below dentate line, more common posteriorly due to more adherent of anoderm to underlying tissue in posterior midline so the blood supply is significantly low as shown by the Doppler flow-metry study<sup>2</sup>. It is estimated that 25% of a women and 8% of a men have anterior fissure<sup>3</sup>. Constipation and passing of hard faces lead to tearing of the mucosa causing pain and bleeding<sup>4</sup>.

The pain of anal fissure is severe and always disproportionate to the severity of physical lesion, it may be so severe that patients may avoid defecation for days until it becomes inevitable, this lead to harden of a

stools, which farther tear the anoderm during defecation<sup>5</sup>. This ulcer is ischemic ulcer and due to hypertonicity of internal anal sphincter due to pain and spasm of sphincter, this causing a vicious cycle and this can lead to chronic anal fissure<sup>6</sup>.

Chronic anal fissure have traditionally managed with lateral internal sphincterotomy or anal dilatation sphincterotomy, however it has been associated with incontinence in up to 35% of patients. Furthermore, this does not take into account normal weakening of the sphincter with age as well as the possibility of future anorectal surgery or obstetrical trauma. Dilatation of the anal canal has also been associated with sphincteric tears and subsequent incontinence<sup>7</sup>. Controlled pneumatic dilatation, however is a variation to the technique that may reduce the risk of sphincter in jury<sup>7</sup>.

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**Corresponding author:**

**Hayder Adnan Fawzi**

Email: hayder.adnan2010@gmail.com

More recently, less invasive strategies have been adopted to induce sphincter relaxation topical agents including nifedipine reduce internal sphincter pressure

and increase blood supply to ischemic ulcer by decreasing the internal anal sphincter tone, and topical agents nifedipine also have anti-inflammatory action. As lidocaine, is the most common topical anaesthetic for anal fissure, which break the vicious cycle of pain<sup>8,9</sup>.

During pregnancy and following childbirth the fissures occur as a superficial split in anterior anoderm may progress to a chronic anal fissure<sup>10</sup>. A typical fissure may be multiple, off the midline, large and irregular, these may be caused by inflammatory bowel disease, local or systemic malignant, venereal infection (syphilis, HIV) trauma, tuberculosis, and chemotherapy<sup>11</sup>. The aim of the current study to evaluate the healing response of the anal fissure to topical application of nifedipine with lidocaine gel, and prevent evolution of acute anal fissure to chronic anal fissure.

## MATERIAL AND METHOD

A prospective study carried out in the surgical outpatient clinic of AL-Diwaniyah teaching hospital from January 2017 to January 2018. The study included one hundred patients, each patients were followed up during the admission period, examination of the anal fissure and its signs, like puckered or spatulated anus, anal sphincter tone by doing per rectum examination (subjective feeling) for the chronic fissure to decided wither its tight or relax, examination for the skin tag (present or absent), and also examination for pressure which indicate the chronicity of anal fissures.

After that the patients were given the formula (cream Nifedipine (0.3%) – lignocaine (1.5%) Combination)<sup>12</sup> and explain to them who to use the formula, the frequency of visit every two weeks to evaluate the response to the formula.

According to the signs and symptoms, the patients were divided into two groups, the first group with acute anal fissure (15 males and 25 females) and second group with chronic anal fissure (25 males and 35 females). In Both groups patients were instructed to apply cream locally into the anal canal twice daily for 3 weeks after defecation<sup>12</sup>.

Anal fissure was defined as acute when its symptoms (moderate to severe pain during defecation, bleeding per rectum) is within 3 to 6 weeks of onset, the patients were assessed with history and physical examination<sup>13</sup>. Chronic anal fissure defined by duration of symptoms

longer than 3 months, the presence of induration at fissure edges, sentinel pile, hypertrophied anal papillae, and circular muscle fibres at the base of the cutaneous defect<sup>14</sup>. The response was shown as stopping or decreasing the bleeding, decreasing the pain, the relaxation of internal anal sphincter and disappearance the induration.

## STATISTICAL ANALYSIS

Analysis of our data done using the software program: SPSS 21 (Statistical Package for Social Sciences). Numeric data were represented by the mean  $\pm$  standard error, while the categorical data represented by numbers and percentages. Independent t-test was used to study the difference between two. For the study of the association between categorical data, the Chi-Square test used. The significant level considered when the P value  $< 0.05$ <sup>9,15</sup>.

## RESULTS

There was no statistically significant difference in the healing rate between acute and chronic lesion, however the rate of healed lesion in acute setting is higher than that of chronic setting (80% vs. 56%)

**Table 1: healing of lesions in male after 6 weeks**

	Healed	Not healed	P value
Acute (15)	12 (80%)	3 (20%)	0.123
Chronic (25)	14 (56%)	11 (44%)	

There was no statistically significant difference in the healing rate between acute and chronic lesion.

**Table 2: healing of lesions in male after 8 weeks**

	Healed	Not healed	P value
Acute (15)	13 (86.7%)	2 (13.3%)	0.591
Chronic (25)	20 (80%)	5 (20%)	

There was no statistically significant difference in the healing rate between acute and chronic lesion, however the rate of healed lesion in acute setting is higher than that of chronic setting (80% vs. 57.1%)

**Table 3: healing of lesions in female after 6 weeks**

	Healed	Not healed	P value
Acute (25)	20 (80%)	5 (20%)	0.064
Chronic (35)	20 (57.1%)	15 (42.9%)	

There was no statistically significant difference in the healing rate between acute and chronic lesion.

**Table 4: healing of lesions in female after 8 weeks**

	Healed	Not healed	P value
Acute (25)	23 (92%)	2 (8%)	0.455
Chronic (35)	30 (85.7%)	5 (14.3%)	

## DISCUSSION

Today, the treatment of chronic anal fissure has become challenging because of irreversible damage and deformation of the internal anal sphincter. Additionally, given that most patients with anal fissure are young and worried about non-voluntary faeces excretion and the consequences after surgery, the use of alternative medicines for treating patients with anal fissure has been of recent concern <sup>16</sup>.

In the current study the healing response of acute anal fissure (AF) after (6 weeks) for both females were 80%, and after extended therapy (8 weeks) the healing response of acute anal fissure for females was 92% and for males were 86.7%, our findings were in agreement with Antropoli et al in which 141 patients treated with nifedipine topically (0.2% nifedipine gel) every 12 hours for three weeks they reported a total remission from acute anal fissure after 21 days of therapy to be 95% <sup>17</sup>. Our findings were in agreement with Digennaro et al in which 171 patients with acute AF treated with Diltiazem gel applied every 12 h for 40 days the rate of efficacy was 89.4 % (complete healing: 64.3 %, improvement: 25.1 %) <sup>18</sup>, also in agreement with Katsinelos et al The effect of topical nifedipine in treatment of acute anal fissure showed that a course of (8 weeks) nifedipine achieved 85.2% remission indicated by resolution of symptoms and healing of fissure and the unhealed 14.8% that 50% undergo lateral internal sphincterotomy and

50% of them continue therapy for four additional weeks that resulting in healing the fissure <sup>19</sup>.

In the current study chronic anal fissure the healing response after (6 weeks) for females were 57.1% (20 patients) and for males were 80% (20 patients), but after extended therapy (8 weeks) the healing response of chronic anal fissure for females were 85.7% (30 patients) and for males were 80% (20 patients). Our findings were in agreement with Digennaro et al in which 171 patients with acute AF treated with Diltiazem gel applied every 12 h for 40 days with chronic fissure the rate of efficacy was 62.8 % (complete healing: 23 %, improvement: 39.8 %) <sup>18</sup>. In a study conducted by Golfam et al, 110 individuals were studied with chronic anal fissure, out of whom 60 were treated with nifedipine and 50 were controls (conventional treatment). In the nifedipine group, 70% of patients achieved recovery (which is in agreement with our findings), and in controls, 12% recovery was observed after four weeks. In the Golfam et al. study, recovery and healing of the pain in the nifedipine group were significantly different from that of the control group <sup>20</sup>.

Oral and topical calcium channel blockers (CCBs) have recently been shown to lower the anal resting pressure by relaxing the internal anal sphincter <sup>21-23</sup>. The transport of calcium through the L-type calcium channels is important for the maintenance of internal anal sphincter tone <sup>24</sup>. As opposed to glyceryl trinitrate, which reduces resting anal tone by releasing nitric oxide, nifedipine (a calcium channel blocker) reduces the tone and spontaneous activity of the sphincter by decreasing the intracellular availability of calcium <sup>24</sup>.

## CONCLUSION

Topical application nifedipine and lidocaine effective in treating acute anal fissures with the healing response of 85%, and prevent evolution of acute anal fissures to chronic anal fissure.

### Conflict of Interest None

**Ethical Clearance:** Informed written consent was obtained from all the participants in the study, and the study and all its procedure were done in accordance with the Helsinki Declaration of 1975, as revised in 2000. Approved by Al-Diwaniyah teaching hospital, department of surgery.

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## REFERENCES

- Nelson R. Non surgical therapy for anal fissure. The Cochrane database of systematic reviews [Internet]. 2006 2006; (4):[CD003431 p.]. Available from: <http://europepmc.org/abstract/MED/17054170> <https://doi.org/10.1002/14651858.CD003431.pub2>.
- Knight JS, Birks M, Farouk R. Topical diltiazem ointment in the treatment of chronic anal fissure. The British journal of surgery. 2001;88(4):553-6. [10.1046/j.1365-2168.2001.01736.x](https://doi.org/10.1046/j.1365-2168.2001.01736.x)
- Madoff RD, Fleshman JW. AGA technical review on the diagnosis and care of patients with anal fissure. Gastroenterology. 2003;124(1):235-45, [https://www.gastrojournal.org/article/S0016-5085\(03\)50035-X/pdf](https://www.gastrojournal.org/article/S0016-5085(03)50035-X/pdf)
- Mancini I, Bruera E. Constipation in advanced cancer patients. Supportive Care in Cancer. 1998;6(4):356-64, <https://link.springer.com/article/10.1007%2Fs005200050177>
- Lund JN, Scholefield JH. Glyceryl trinitrate is an effective treatment for anal fissure. Diseases of the colon and rectum. 1997;40(4):468-70,
- McCallion K, Gardiner K. Progress in the understanding and treatment of chronic anal fissure. Postgraduate medical journal. 2001;77(914):753-8, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1742193/pdf/v077p00753.pdf>
- Tranqui P, Trottier DC, Victor JC, Freeman JB. Nonsurgical treatment of chronic anal fissure: nitroglycerin and dilatation versus nifedipine and botulinum toxin. Canadian Journal of Surgery. 2006;49(1):41-5, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3207506/> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3207506/pdf/20060200s00009p41.pdf>
- Hang MTH, Smith BE, Keck C, Keshavarzian A, Sedghi S. Increasing efficacy and reducing side effects in treatment of chronic anal fissures: A study of topical diazepam therapy. Medicine. 2017;96(20):e6853. [10.1097/MD.00000000000006853](https://doi.org/10.1097/MD.00000000000006853)
- Mohammed MA, Kadhim KA, Jasim GA, Fawzi HA. Metformin compared to insulin for the management of gestational diabetic. Int J Res Pharm Sci. 2018;9(3):1063-7. <https://doi.org/10.26452/ijrps.v9i3.1630>
- Patel JR, Dudhamal TS. A comparative clinical study of Yashtimadhu Ghrita and lignocaine-nifedipine ointment in the management of Parikartika (acute fissure-in-ano). Ayu. 2017;38(1-2):46-51. [10.4103/ayu.AYU\\_93\\_17](https://doi.org/10.4103/ayu.AYU_93_17)
- Sigle GW, Kim R. Sexually Transmitted Proctitis. Clinics in Colon and Rectal Surgery. 2015;28(2):70-8. [10.1055/s-0035-1547334](https://doi.org/10.1055/s-0035-1547334)
- Singh B, Khichy S, Kumar A, Singh S, Neki N. COMPARATIVE STUDY TO OBSERVE EFFECTS OF TOPICAL NIFEDIPINE WITH LIGNOCAINE AND TOPICAL SUCRALFATE WITH LIGNOCAINE IN ACUTE ANAL FISSURE. Journal of Advanced Medical and Dental Sciences Research. 2016;4(6):81,
- Hafeez U, Choudhry M, Khan S. Comparison of Healing Rate between Surgical and Nonsurgical Management of Acute Anal Fissure. PAKISTAN JOURNAL OF MEDICAL & HEALTH SCIENCES. 2016;10(4):1414-6,
- Sonarkar RK, Deshmukh SD, Akhtar MA, Bindlish R. Segmental lateral internal Sphincterotomy: a new technique for treatment of chronic anal fissure-clinical outcome and review of literature. IJSS. 2016;2(3):30,
- Yahya RN, Kasim AA, AlGawwam G, A. Fawzi H. Treatment satisfaction with disease-modifying therapy in relapsing-remitting multiple sclerosis in Iraq. International Journal of Research in Pharmaceutical Sciences. 2018;9(3):836-43. <https://doi.org/10.26452/ijrps.v9i3.1578>
- Khaledifar B, Mahmoudi MYA, Mobasheri M. A Double-Blind Randomized Trial Comparing the Effectiveness and Safety of Nifedipine and Isosorbide Dinitrate in Chronic Anal Fissure. The Malaysian Journal of Medical Sciences : MJMS. 2015;22(5):42-9, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5295740/> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5295740/pdf/mjms-22-5-042.pdf>
- Antropoli C, Perrotti P, Rubino M, Martino A, De Stefano G, Migliore G, et al. Nifedipine for local

- use in conservative treatment of anal fissures: preliminary results of a multicenter study. *Diseases of the colon and rectum*. 1999;42(8):1011-5,
18. Digennaro R, Pecorella G, La Manna S, Alderisio A, Alderisio A, Jr., De Pascalis B, et al. Prospective multicenter observational trial on the safety and efficacy of LEVORAG(R) Emulgel in the treatment of acute and chronic anal fissure. *Techniques in coloproctology*. 2015;19(5):287-92.10.1007/s10151-015-1289-2
19. Katsinelos P, Kountouras J, Paroutoglou G, Beltsis A, Chatzimavroudis G, Zavos C, et al. Aggressive treatment of acute anal fissure with 0.5% nifedipine ointment prevents its evolution to chronicity. *World Journal of Gastroenterology : WJG*. 2006;12(38):6203-6.10.3748/wjg.v12.i38.6203
20. Golfam F, Golfam P, Khalaj A, Sayed Mortaz SS. The effect of topical nifedipine in treatment of chronic anal fissure. *Acta medica Iranica*. 2010;48(5):295-9, <http://acta.tums.ac.ir/index.php/acta/article/download/4051/4026>
21. Agaoglu N, Cengiz S, Arslan MK, Turkyilmaz S. Oral nifedipine in the treatment of chronic anal fissure. *Digestive surgery*. 2003;20(5):452-6.10.1159/000072715
22. Perrotti P, Bove A, Antropoli C, Molino D, Antropoli M, Balzano A, et al. Topical nifedipine with lidocaine ointment vs. active control for treatment of chronic anal fissure: results of a prospective, randomized, double-blind study. *Diseases of the colon and rectum*. 2002;45(11):1468-75.10.1097/01.dcr.0000029705.79796.53
23. Ho KS, Ho YH. Randomized clinical trial comparing oral nifedipine with lateral anal sphincterotomy and tailored sphincterotomy in the treatment of chronic anal fissure. *The British journal of surgery*. 2005;92(4):403-8.10.1002/bjs.4882
24. Cook TA, Brading AF, Mortensen NJ. Differences in contractile properties of anorectal smooth muscle and the effects of calcium channel blockade. *The British journal of surgery*. 1999;86(1):70-5.10.1046/j.1365-2168.1999.00998.x