Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2024i1.782
*Biol. Clin. Sci. Res. J., Volume, **2024**: 782*
Original Research Article

COMPARISON OF EFFECTIVENESS OF TOPICAL NIFEDIPINE AND DILTIAZEM IN THE TREATMENT OF ANAL FISSURES

SADIA, NASEER S*, FAROOQI A, ZULFIKAR I, SAEED S, SHAH HH

Department of General Surgery, DUHS, Dr Ruth K. M. Pfau Civil Hospital, Karachi, Pakistan
**Corresponding author's email address:* shafqnaseer24@gmail.com

(Received, 15th December 2023, Revised 18th March 2024, Published 4th April 2024)

Abstract: *Anal fissure, a tear in the anal canal below the dentate line, is commonly managed pharmacologically as the primary approach, with surgery considered secondary.* ***Objective:*** *To compare the efficacy of topical nifedipine and diltiazem in the prompt resolution of pain and bleeding associated with anal fissure management.* ***Methods:*** *A prospective cohort study was conducted at Dr. Ruth K. M. Pfau Civil Hospital, Karachi, from June 2023 to November 2023. One hundred patients with anal fissures were randomly allocated into two groups: Group N (Nifedipine) and Group D (Diltiazem). Topical medication was administered until healing occurred. The visual analogue scale (VAS) assessed the patient's progress in terms of bleeding and pain. Side effects were monitored. Statistical analysis included an independent t-test for comparing VAS scores and a post-stratification chi-square test for associations between bleeding, side effects, and other variables.* ***Results:*** *At baseline, mean pain scores were 8.30±0.90 in group D and 7.78±1.29 in group N. At the first follow-up, mean pain scores were 5.58±1.34 in group D and 4.56±1.48 in group N, with a significant difference (p<0.001). Bleeding did not significantly decrease at the first follow-up but decreased significantly at the subsequent follow-ups in both groups. Side effects did not differ significantly between groups.* ***Conclusion:*** *Topical nifedipine is more effective than diltiazem for managing anal fissures in terms of pain reduction. However, both medications showed comparable efficacy in reducing bleeding, with no significant difference in side effects observed.*

Keywords: Anal Fissures, Bleeding, Diltiazem, Effectiveness, Nifedipine, Pain

Introduction

One of the most prevalent anorectal illnesses, the anal fissure, is linked to a worse quality of life and decreased productivity. An anal fissure is defined as a tear or ulcer that develops in the skin of the anal margin (1-3). Extreme discomfort (sometimes lasting up to two hours after defecation) and bleeding are common symptoms of anal fissures. Anal fissures are divided into classes. Acute occurs in less than six weeks, whereas chronic fissures occur in more than six weeks (2). Fissures are classified according to the tears and splits' location, size, form, volume, and healing duration. Primary fissures are benign and situated in the posterior or anterior region; secondary fissures, on the other hand, are characterized by lateral or numerous rips, which frequently point to a more significant underlying condition (4, 5).

The diagnosis of chronic anal fissures is solely clinical, based on the visibility of fibers of the sphincter at the base of the fissure, anal papillae, sentinel piles, and indurated edges (6, 7). Anal fissures can result in infection, abscesses, or recurrence if they are not well managed. They may also result in fecal impaction when patients refrain from feces, in addition to lowering their general quality of life (8). Anal fissures are thought to affect 11% of people in their lifetime, and both men and women are equally vulnerable (9).

Although fissures can develop at any age, they most frequently affect younger and middle-aged individuals, with a mean onset age of 39 (8, 10, 11). Anal fissures' pathogenesis is not understood. High resting anal sphincter pressure is thought to be caused by acute damage to the anoderm during the passage of hard or big feces, diarrhea, anorectal surgery, and anal intercourse. This injury causes local discomfort and spasm of the internal anal sphincter (12). This ultimately causes ischemia and decreased blood flow, delaying the healing of the fissure (13).

The treatment options for anal fissures are as varied as the disorder itself, ranging from non-operative methods like sitz baths, topical ointments, Botulinum toxin injections, and dietary adjustments to surgical methods if non-operative therapies and medications prove to be futile.5 Reducing the resting pressure of the internal anal sphincter (IAS) and enhancing blood flow in the ischemic region are the primary objectives of AAF therapy (1).

When Chrysos et al. examined the impact of calcium channel blockers (CCBs) on the anal sphincter for the first time in 1996, they found that the anal resting pressure was reduced by over 30%.15 The American Society of Colon and Rectal Surgeons (ASCRS) recommends that non-surgical treatment, especially with a pharmacological agent such as topical glyceryl trinitrate and calcium channel blockers, must be considered as the first-line therapy (14, 15). Currently, topical treatment with glyceryl trinitrate is widely used for the management of anal fissures with healing of up to 80%, although 20-30% of patients discontinue their treatment (16) because of various side effects like headache, postural hypotension, flushing, allergy.18-20 Also, a high recurrence rate of 50% was reported (13).

Calcium channel blockers, like diltiazem and nifedipine, are nitrogen oxide alternative therapeutics with fewer side effects. Eight calcium channel blockers reduce muscle tone by increasing blood flow (17). An updated Cochrane review published in 2012 reported that calcium channel blockers (nifedipine and diltiazem) and glyceryl trinitrate have the

[Citation: Sadia., Naseer, S., Farooqi, A., Zulfikar, I., Saeed, S., Shah, H.H. (2024). Comparison of effectiveness of topical nifedipine and diltiazem in the treatment of anal fissures. *Biol. Clin. Sci. Res. J.*, **2024***: 782*. doi: https://doi.org/10.54112/bcsrj.v2024i1.782]

same effect on fissure healing (16). However, calcium channel blockers have fewer side effects, so some physicians prefer to prescribe calcium channel blockers for the treatment of anal fissures (18). Although all calcium channel blockers are from the same drug class, they contain heterogeneous compounds and have different chemical structures, so their potency for blocking calcium channels will differ. Diltiazem potentially inhibits calcium function in the cardiac and vascular smooth muscle cells, while nifedipine is more potent in relaxing peripheral smooth muscle cells (19).

Nifedipine and diltiazem efficacy for treating anal fissures have been evaluated separately in various studies. Kujur and colleagues showed that these two drugs had the same effect in the management of chronic anal fissures (20); however, the number of studies focused on the application of these drugs for the treatment of AAFs is limited.

The purpose of this study is to evaluate and compare the effectiveness of topical nifedipine and topical diltiazem in treating patients with anal fissures.

Methodology

This cohort study was carried out prospectively at Dr Ruth K. M. Pfau Civil Hospital, Karachi, from June 2023 to November 2023. The research proposal was approved by the Research Committee and the hospital's Ethical Committee. Participants were explained about the study purpose and associated risks and benefits of the procedure to obtain their consent. Informed and written consent was also taken from the participants before enrollment in the study. The sample size for this study was determined with the help of OpenEpi. Non-probability consecutive sampling was used for sample selection. Patients with anal fissures associated with an underlying condition such as diabetes mellitus, hypertension, malignancy, anemia, inflammatory bowel disease, hemorrhoids, and persistent diarrhea were not included in the study. A total of a hundred participants who followed the inclusion criteria were part of the current study and were divided randomly into two groups of equal participants. Anal fissure caused by trauma to the anal canal, often due to constipation or hard stool, was considered a Primary Fissure. An anal fissures caused by underlying diseases like inflammatory bowel disease or HIV infection were considered as Secondary fissures. An anal fissure that does not heal on its own and requires medical intervention, such as topical medication or surgery, is considered a Non-healing Fissure. Non-healing fissures may be associated with chronic anal pain and discomfort. In Group N, patients were given topical Nifedipine; in Group D, patients were given topical Diltiazem. Both medications, i.e., nifedipine and diltiazem, were administrated topically and three times a day until healing. The cream was applied by the patients themselves with the fingertip, inside and circumferentially around the anus. Patients were examined every two weeks for a minimum of 6 weeks, a routine follow-up. Patients who could not attend on the scheduled dates were contacted via phone and enquired about their progress. They were assessed for bleeding and pain, which was concluded in the healing status. Pain was evaluated on a visual analog scale (VAS scale). Furthermore, possible side effects of the medication were monitored, such as hypotension, headache, and rash. Confidentiality of the participants was maintained throughout the study. Their record number was tagged with other serial numbers to conceal the patient's identity, and only the principal investigator had access to the original data. The variables were recorded in the predesigned proforma.

Data was analyzed using SPSS V-23. Qualitative data were presented as frequencies and percentages. Quantitative variables were summarized as mean±SD for normality distributed data or median with inter-quartile range for non-normally distributed data. VAS score was compared using an independent t-test. Stratification was done, and the post-stratification chi-square test was applied to find the association of bleeding and side effects with other variables, considering the P value less than or equal to 0.05 as significant.

Results

In our study, 70.0% of male and 30.0% of female patients were in group D; however, 62.0% of male and 38.0% of female patients were in group N. The overall mean age was 39.86±10.99 years in group D and 39.34±9.27 years in group N. Among patients in group D, 62.0% of patients belonged to the age ≤40 years, and 38.0% of patients were aged >40 years; however, among patients in group N, 56.0% of patients belonged to the age ≤40 years, and 44.0% of patients were aged >40 years. The mean pain score at baseline was 8.30±0.90 in group D and 7.78±1.29 in group N. The difference in pain score was found to be statistically significant (p=0.023). It was observed at baseline that all patients of group D had severe pain (score 7-10); however, in group N, 16.0% had moderate pain (score 4-6), and 84% of patients had severe pain (score 7-10). Bleeding was observed in 94% of patients and 80% of patients in groups D and N, respectively. This was statistically significant between the two medicines (p=0.037). The results are also presented in Table 1.

Table 1: Frequency of demographic characteristics and baseline findings

	Diltiazem	Nifedipine	*P-value*
Gender			
Male	35(70%)	31(62%)	0.398**
Female	15(30%)	19(38%)	
Age	39.86±10.99	39.34±9.27	0.799**
Age ≤ 40 years	31(62.0)	28(56.0)	0.452**
Age > 40 years	19(38.0)	22(44.0)	
Baseline Pain	8.30±0.90	7.78±1.29	0.023*
Moderate Pain	0 (0.0%)	8 (16.0%)	0.006*
Severe Pain	50 (100.0%)	42 (84.0%)	
Baseline Blooding			
Present	47(94%)	40(80%)	0.037*
Absent	3(6%)	10(20%)	

*Independent t-tests and Chi-square tests were applied * Significant at 0.01 levels **Not Significant at 0.05 levels*

[Citation: Sadia., Naseer, S., Farooqi, A., Zulfikar, I., Saeed, S., Shah, H.H. (2024). Comparison of effectiveness of topical nifedipine and diltiazem in the treatment of anal fissures. *Biol. Clin. Sci. Res. J.*, **2024***: 782*. doi: https://doi.org/10.54112/bcsrj.v2024i1.782]

As far as side effects are concerned, headache was observed in 4% of patients in group D and 2% of patients in group N. The itching was observed in 4% of patients in group D and also 4% of patients in group N. There was no statistically significant difference in side effects between the two medicines (p=1.000), as presented in Table 2.

Table 2: Frequency and association of side effects

Side Effects	Diltiazem	Nifedipine	*P-value*
Headache	2 (4.0%)	1 (2.0%)	1.0000**
Itching	2 (4.0%)	2 (4.0%)	
*Fisher Exact Test was applied. ** Not Significant at 0.01 levels.*			

The results showed that the mean pain score at 1st follow-up was 5.58±1.34 in group D and 4.56±1.48in group N. The difference in pain score was found to be statistically significant (p<0.001). 10% of patients had mild pain (score 1-3), 60% of patients had moderate pain (score 4-6), and 30% of patients had severe pain (score 7-10) in Group D. In group N, 20% of patients had mild pain (score 1-3), 74% of patients had moderate pain (score 4-6), and 6% of patients had severe pain (score 7-10). The results of 2nd follow-up show that mean pain was 1.38±1.33 in group D and 1.08±1.20 in group N. The difference in pain score was not statistically significant (p=0.242). 90% of patients had mild pain (score 1-3), and 10% of patients had moderate pain (score 4-6) in group D. In group N, 98% of patients had mild pain (score 1-3), and 2% of patients had moderate pain (score 4-6). The 3rd follow-up shows that mean pain was 0.26±0.56 in group D and 0.14±0.35 in group N. This pain score was also not statistically significant (p=0.205). The pain was reduced to mild in all patients of group D as well as group N. The difference in pain score was found to be statistically insignificant (p=205). The results are also presented in Table 3**.**

At 1st follow-up, bleeding decreased in 62% of patients and subsided in 32% of patients of group D. In group N, bleeding decreased in 48% of patients and subsided in 32% of patients. This was not statistically significant between the two medicines (p=0.097). In 2nd follow-up, bleeding decreased in 48% of patients and subsided in 46% of patients of group D. In group N, bleeding decreased in 18% of patients and subsided in 62%. This was statistically significant between the two medicines (p=0.003). However, in 3rd follow-up, bleeding was decreased in all patients and subsided in all 94% of patients of group D who observed bleeding at baseline. In group-N, bleeding was also decreased in all patients and subsided in all 80% of patients of group-N who observed bleeding at baseline. This was also statistically significant between the two medicines (p=0.037). The results are presented in Table 4.

Table 3: Mean difference of pain score at different follow-ups between two medicines

	Diltiazem	Nifedipine	*P-value*
At 1st Follow-up	5.58±1.34	4.56±1.48	<0.001*
At 2nd Follow-up	1.38±1.33	1.08±1.20	0.242**
At 3rd Follow-up	0.26±0.56	0.14±0.35	0.205**
*An independent t-test was applied, which was * Significant at 0.01 levels **Not Significant at 0.05 levels.*			

Table 4: Association of bleeding at different follow-ups between two medicines

	Diltiazem	Nifedipine	*P-value*
At 1st Follow-up			
Decrease	31(62%)	24(48%)	0.097**
Subside	16(32%)	16(32%)	
Absent	3(6%)	10(20%)	
At 2nd Follow-up			
Decrease	24(48%)	9(18%)	0.003*
Subside	23(46%)	31(62%)	
Absent	3(6%)	10(20%)	
At 3rd Follow-up			
Decrease	0(0)	0(0)	0.037*
Subside	47(94%)	40(80%)	
Absent	3(6%)	10(20%)	
*The Chi-square Test was applied * Significant at 0.01 levels **Not Significant at 0.05.*			

Discussion

Treatment of anal fissures is still tricky. Due to the risk of infection and incontinence following surgery, among other consequences, nowadays, the world has shifted to medicinal treatments from surgical treatments (21). nitroglycerin ointment can relax the sphincter muscle, but adverse effects, including excruciating headaches, limit their administration (22). As a result, calcium drugs such as topical diltiazem and calcium channel blockers were developed (23, 24). Numerous non-operative methods have been demonstrated to be beneficial for anal fissures management. Some treatment options include topical gels, creams, and ointments. The disorder can be effectively managed with several approaches, such as topical gels containing Glyceryl Trinitrate, Lidocaine Hydrochloride (LDH), Diltiazem Betamethasone Valerate (BMV), and Hydrochloride, a combination of Nifedipine (NIF), as well as calcium blockers that can be taken orally and applied topically and Botulinum toxin injections (4).Results from a study (10)

[Citation: Sadia., Naseer, S., Farooqi, A., Zulfikar, I., Saeed, S., Shah, H.H. (2024). Comparison of effectiveness of topical nifedipine and diltiazem in the treatment of anal fissures. *Biol. Clin. Sci. Res. J.*, **2024***: 782*. doi: https://doi.org/10.54112/bcsrj.v2024i1.782]

unmistakably show that topical Diltiazem or Nifedipine produces substantially superior pain relief, quicker bleeding control, and faster healing. They also observed that Diltiazem and Nifedipine had no statistically significant difference; nonetheless, Diltiazem was linked to a considerably higher frequency of perianal dermatitis than Nifedipine. The same study also found that most patients were in the twenty- to forty-year-old age range and that the frequency was higher in men than women. After only one week of therapy, researchers found that the pain levels on the Nifedipine and Diltiazem arms were considerably improved when comparing the VAS values. Both the Diltiazem and Nifedipine groups saw a substantial improvement in bleeding after two weeks of therapy (10).

Another study showed that the application of nifedipine was more efficient in pain relief and remission rate compared with diltiazem. The side effects were rarely reported by the patients in both groups, and side effects were not significantly different between the two drugs (1).

Calcium ions have a fundamental function in the maintenance of basal internal anal sphincter (IAS) tone (25). CCBs inhibit calcium influx within the cell through voltage-gated L-type calcium channels in smooth muscle myocytes, thereby relaxing the smooth muscle and enhancing blood perfusion. The boosted blood supply in the anal fissure area facilitates the healing process (26). In a study by Kujur and colleagues, topical nifedipine or diltiazem was introduced as an effective treatment method.30 Accordingly, a higher healing rate was reported compared with the results of a study by Sanat MZ (1).

According to the results of other studies, an acceptable healing rate was reported for applying topical CCBs such as nifedipine or diltiazem as a first-line treatment method (23, 27). There is a difference between the remission rates reported in the earlier studies. This disagreement could be related to differences in drug concentration, intervention duration, or the participants' characteristics. Few clinical trials have been conducted to compare the effect of nifedipine or diltiazem (10).

In a study by Antropoli and colleagues, 141 patients were given topical 0.2% nifedipine gel, and 142 patients were given topical lignocaine 1% and hydrocortisone acetate gel 1% every 12 hours for three consecutive weeks. The remission rate in the nifedipine group was 95%, whereas in the control group, the remission rate was only 50% (28). Also, Akıncı et al. evaluated the treatment and recurrence prevention in 100 participants who randomly received two different treatment methods, 0.2% glyceryl trinitrate versus 0.5% topical nifedipine, for 21 days. Symptomatic relief and the healing rate of the nifedipine group were higher than the glyceryl trinitrate group (56% and 86% versus 22% and 64%, respectively) (29).

Studies that evaluated nifedipine for fissure treatment have reported headaches.36 In another study, fissure treatment with topical diltiazem was associated with hypotension in 10%, fibrosis in 15%, skin tag in 15% of participants, and headache (30). Based on the results of another study, (1) in the nifedipine group, flushing, dizziness, hypotension, and heartbeat were reported. In the diltiazem group, the side effects were headaches and dizziness.

The limited sample size in this study limits its usefulness. The study's limitations include the lack of a control group, a short follow-up time, and no patient characteristics that may be risk factors evaluated. The duration of the therapy with topical medicines was extended, resulting in lower patient compliance throughout follow-up. Because the study was conducted in an urban setting, the findings may not apply to broader populations.

Conclusion

The results of the current study for the treatment of anal fissures with topical diltiazem and topical nifedipine demonstrated that topical nifedipine compared with topical diltiazem is significantly more effective in reducing pain and bleeding. It was also observed that topical nifedipine and diltiazem were not different regarding CCB-related side effects.

Hence, it can be concluded that in the treatment of anal fissure, topical Nifedipine seems superior to the treatment anal fissure with topical Diltiazem. However, the topical use of CCBs as first line for the management of anal fissures is recommended.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (KKPFP-ERC-22-0001)

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

SADIA (Postgraduate Trainee)
Coordination of collaborative efforts.
Conception of Study, Final approval of manuscript.
SHAFAQ NASEER (Assistant Professor)
Study Design, Review of Literature.
Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, and final approval.
AIMAN FAROOQI (Postgraduate Trainee)
Manuscript revisions, critical input.
Coordination of collaborative efforts.
IMRANA ZULFIKAR (Professor)
Data acquisition and analysis.
Manuscript drafting.
SUMMAYA SAEED (Associate Professor)
Data entry and data analysis, as well as drafting the article.
Coordination of collaborative efforts
HUSSAIN HAIDER SHAH
Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, and final approval.

References

1. Sanat ZM, Ganjaroudi NM, Mansouri M. The Effect of Topical Nifedipine versus Diltiazem on the Acute Anal Fissure: A Randomized Clinical Trial. Middle East Journal of Digestive Diseases. 2023;15(2):121.
2. Newman M, Collie M. Anal fissure: diagnosis, management, and referral in primary care. The British Journal of General Practice. 2019;69(685):409.
3. Navarro-Sánchez A, Luri-Prieto P, Compañ-Rosique A, Navarro-Ortiz R, Berenguer-Soler M, Gil-Guillén VF, et al. Sexuality, Quality of Life, Anxiety, Depression, and Anger in Patients with Anal Fissure. A Case–Control Study. Journal of Clinical Medicine. 2021;10(19):4401.
4. ANSARI NA, BHORE A, MUSA O. A Comparative Study of Topical Diltiazem (2%) with Topical Glyceryl Trinitrate (0.2%) as a Conservative Treatment for Anal Fissure. Journal of Clinical & Diagnostic Research. 2020;14(7).
5. Villalba H, Villalba S, Abbas MA. Anal fissure: a common cause of anal pain. Perm J. 2007;11(4):62-5.
6. Sierra-Arango F, De la Hoz-Valle J, Espinosa JP, Moreno-Montoya J, Vásquez Roldan M, Pérez-Riveros ED. Clinical Outcomes of Medical Management Options for Chronic Anal Fissures in a Long-Term Follow-up: Systematic Review and Meta-Analysis. Digestive Diseases. 2023;41(5):822-32.
7. Goligher JC. Surgery of the anus, rectum and colon. Bailliere Tindall. 1980:924-5.
8. Sailer M, Bussen D, Debus E, Fuchs K, Thiede A. Quality of life in patients with benign anorectal disorders. British Journal of Surgery. 1998;85(12):1716-9.
9. Cross K, Massey E, Fowler A, Monson J. The management of anal fissure: ACPGBI position statement. Colorectal Dis. 2008;10(Suppl 3):1-7.
10. Kujur ADS, Ekka NMP, Chandra S, Lal S, Malua S. Comparative study to assess the effectiveness of topical nifedipine and diltiazem in the treatment of chronic anal fissure. Journal of Family Medicine and Primary Care. 2020;9(11):5652-7.
11. Hananel N, Gordon PH. Re-examination of clinical manifestations and response to therapy of fissure-in-ano. Diseases of the colon & rectum. 1997;40(2):229-33.
12. Keck JO, Staniunas RJ, Coller JA, Barrett RC, Oster ME. Computer-generated profiles of the anal canal in patients with anal fissure. Diseases of the colon & rectum. 1995;38(1):72-9.
13. Chrysos E, Xynos E, Tzovaras G, Zoras OJ, Tsiaoussis J, Vassilakis SJ. Effect of nifedipine on rectoanal motility. Diseases of the colon & rectum. 1996;39:212-6.
14. Schouten WR, Briel JW, Auwerda JJ. Relationship between anal pressure and anodermal blood flow: the vascular pathogenesis of anal fissures. Diseases of the colon & rectum. 1994;37:664-9.
15. Klosterhalfen B, Vogel P, Rixen H, Mittermayer C. Topography of the inferior rectal artery: a possible cause of chronic, primary anal fissure. Diseases of the colon & rectum. 1989;32(1):43-52.
16. Recamier J. Extension, massage et percussion cadancee dans le traitment des contractures musculaires. Rev Med. 1838;1:74-89.
17. Lockhart-Mummery JP. Diseases of the rectum and colon and their surgical treatment. (No Title). 1934.
18. Bennett R, Goligher J. Results of internal sphincterotomy for anal fissure. British medical journal. 1962;2(5318):1500.
19. 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 & rectum. 2002;45:1468-75.
20. Carapeti EA, Kamm MA, Phillips RK. Topical diltiazem and bethanechol decrease anal sphincter pressure and heal anal fissures without side effects. Diseases of the colon & rectum. 2000;43(10):1359-62.
21. Sanei B, Mahmoodieh M, Masoudpour H. Comparison of topical glyceryl trinitrate with diltiazem ointment for the treatment of chronic anal fissure: a randomized clinical trial. Acta Chirurgica Belgica. 2009;109(6):727-30.
22. Utzig M, Kroesen A, Buhr H. Concepts in pathogenesis and treatment of chronic anal fissure—a review of the literature. Official journal of the American College of Gastroenterology| ACG. 2003;98(5):968-74.
23. Nordholm-Carstensen A, Perregaard H, Wahlstrøm KL, Hagen KB, Hougaard HT, Krarup P-M. Treatment of chronic anal fissure: a feasibility study on Levorag® Emulgel versus Diltiazem gel 2%. International Journal of Colorectal Disease. 2020;35:615-21.
24. Bulus H, Varol N, Tas A, Coskun A. Comparison of topical isosorbide mononitrate, topical diltiazem, and their combination in the treatment of chronic anal fissure. Asian Journal of Surgery. 2013;36(4):165-9.
25. Jones OM, Brading AF, Mortensen NJ. The physiology, pharmacology and therapeutic manipulation of the internal anal sphincter. Canadian Journal of Gastroenterology and Hepatology. 2002;16:249-57.
26. Sahebally SM, Ahmed K, Cerneveciute R, Iqbal A, Walsh SR, Joyce MR. Oral versus topical calcium channel blockers for chronic anal fissure-a systematic review and meta-analysis of randomized controlled trials. International Journal of Surgery. 2017;44:87-93.
27. Jin JZ, Hardy M-O, Unasa H, Mauiliu-Wallis M, Weston M, Connolly A, et al. A systematic review and meta-analysis of the efficacy of topical sphincterotomy treatments for anal fissure. International Journal of Colorectal Disease. 2022:1-15.
28. 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 & rectum. 1999;42(8):1011-5.
29. Akıncı O, Abdulrahman S, Güngör Ö, Yüceyar NS, Perek A, Ertürk MS. Randomized comparison of the effect of 0.2% glyceryl trinitrate and 0.5% topical nifedipine in acute anal fissure treatment. Turk J Colorectal Dis. 2020;30(4):246-52.
30. MOHAB GE, WASFY HA, ABDEL-MAKSOUD M, IBRAHIM M. Comparative Study between the Use of Topical GlycerylTrinitrate Vs. Topical Diltiazem in Treatment of Acute Anal Fissure. The Medical Journal of Cairo University. 2021;89(March):69-76.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/. © The Author(s) 2023

[Citation: Sadia., Naseer, S., Farooqi, A., Zulfikar, I., Saeed, S., Shah, H.H. (2024). Comparison of effectiveness of topical nifedipine and diltiazem in the treatment of anal fissures. *Biol. Clin. Sci. Res. J.*, **2024***: 782*. doi: https://doi.org/10.54112/bcsrj.v2024i1.782]