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Comparative Efficacy of Topical Metronidazole and Diltiazem versus Diltiazem Alone in the Treatment of Acute Anal Fissure

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A B S T R A C T

Background: Acute anal fissure (AAF) is a disease associated with intense perianal pain and secondary muscle guarding. Traditional treatment focuses on muscle relaxation, but recent evidence indicates that subclinical bacterial colonization and local inflammation play a major role in hindering tissue repair.

Objectives: The research was to see the difference in the clinical outcomes of 1 per cent Metronidazole and 2 per cent Diltiazem cocktail versus the classical 2 per cent of Diltiazem monotherapy.

Methodology: The study was a randomized controlled trial conducted at the General Surgery Department of the Divisional Headquarters Teaching Hospital, Mirpur from (28-07-2025 to 02-02-2026). Sixty adults (18 to 70 years) who had acute fissures were recruited. The combination treatment was given to Group A, whereas standard Diltiazem monotherapy was given to Group B. Healing, pain (assessed using a Visual Analog Scale), and rectal bleeding were observed over a period of more than 6 weeks during which patients received twice-daily applications. The level of statistical significance was $p < 0.05$.

Results: The combination therapy showed a 40% superior healing rate. Complete recovery was achieved by 86.7% in Group A compared to 46.7% in Group B ($p = 0.001$). Mean VAS scores in Group A dropped significantly to 1.23 ± 1.63, whereas Group B remained higher at 2.73 ± 1.76 ($p < 0.001$). Persistent bleeding was significantly lower in the combination group (3.3%) than in the control (30%).

Conclusion: It is much more effective to treat infection and inflammation with muscle spasms than to treat spasms only. Dual therapy is a better non-surgical standard of care that enhances patient safety and outcomes.

Key Words: Acute Anal Fissure, Chemical Sphincterotomy, Diltiazem, Fissure Healing, Metronidazole

Introduction

Acute anal fissure is a condition which has become one of the most commonly diagnosed in the field of rectal specialists across the globe, which is commonly linked to chronic anal pain, blood loss, and that it contributes to the substantial decline of the quality of life of patients.[1] Lateral internal sphincterotomy has been termed as the most prevalent intervention of treatment in non-healing and persistent cases, it is associated with the development of bowel taboo loss, and long-term results have been reported to be 3-45 per cent. This complication has demonstrated the necessity to pay more attention to chemical sphincterotomy.[2,3] The use of antihypertensives like Diltiazem has become a common practice due to the fact that it relaxes the internal anal sphincter and also improves blood flow to the region thus promoting wound healing.[4,5] Because of its inconsistency, there is still a significant percentage of patients that do not respond to medical interventions alone without an increase in the wound repair. This leads to the emergence of a number of people who experience incurable symptoms, end up paying more in medical expenses, and, in other instances, undergo surgical procedures. Most recent studies have also reported that bacterial factors and occult infections may impair fissure healing by promoting the development of protective layers and local tissue swelling.[6,7]

Some studies have tried to overcome this shortcoming and have shown more positive clinical outcomes. In one of these studies, the introduction of topical metronidazole into routine therapy resulted in significant improvement in healing, increasing recovery rates to 82 per cent compared with 42 per cent.[6,8] Similarly, research by another group has shown that adding antibiotics to the treatment regimen not only reduced the total healing time but also improved pain management compared with vasodilators alone.[9,10] The opposite is true since Elgendy et al. (2024) did not

report similar advantages. The difference between the two things shows that various medical factors play a role. Different types of bacteria in the environment also determine how well treatment methods work.[11,12]

The findings show that more local studies are needed. This study helps determine which treatments work best across different groups. Due to the inability to always resort to surgery and the desire of people not to lose bowel control, it is highly important to make medical treatment as efficient as possible.

Methodology

This study was a randomized controlled trial conducted at the Divisional Headquarters Teaching Hospital in Mirpur, AJK, spanning six months from July 28, 2025, to February 2, 2026. Ethical approval was obtained from the Hospital Ethics Committee, and all participants provided written informed consent prior to enrollment. Sixty patients were selected by us, adequate to achieve 95% confidence with a 5% margin of error, based on findings from other studies on healing rates.

Participants were not selected at random; we brought them in sequentially when they appeared. In order to qualify, the subjects were required to be men or women within the age range of 18 to 70, suffering from a recent anal fissure and a minimum pain score of 6. Symptoms lasted less than six weeks, and all were set for non-surgical treatment. The research excluded patients who had permanent fissures or had undergone anal surgery, or who had intestinal disorders, or who were pregnant, or who had allergic reactions to the study medications. One doctor provided all treatments to maintain consistency, and standard care was followed. After 6 weeks, a senior resident checked if the patients had healed, without knowing which group they were in. Healing meant the fissure was fully closed. This helped avoid bias. The main researcher recorded all results.

Results

The study was done on 60 patients who were treated and presented themselves at the General Surgery Department of the Divisional Headquarters Teaching Hospital in Mirpur, Azad Jammu and Kashmir. The average age of the group was 44.2 years, with 32 men and 28 women accounting for 53.3 percent and 46.7 percent, respectively, of the population. Each group had 30 patients. The two groups had similar age distributions, with Group A and Group B having average ages of 44 and 44.4, respectively. The results showed no significant differences between the two groups.

Bowel irregularity occurred frequently. Considering all the patients, 35 (approximately 58%) had difficulty with hard stools, 60% within Group A, 56.7% in Group B. Something out of the ordinary appeared regarding the location of the fissures: 38.3% was observed at the front (anterior), and 30% of the patients presented with multiple fissures. You can find all the details in Tables 1 and 2. At this moment, refer to the third table regarding healing rates. Cohort A achieved far superior results. More patients fully recovered in Group A than in Group B. In Group B, only 14 patients (46.7%) achieved complete recovery, while in Group A, 26 patients (86.7%) did (30 out of 30). Pain scores also differed between the two groups. Group A's average dropped from 8.37 to 1.23. Group B improved less, as their scores went from 8.30 to 2.73. One can spot those exact numbers in Table 4. Rectal hemorrhage did not completely resolve, but it occurred in only 1 person in Group A (3.3%). In Group B, it stuck around for 9 people, or 30% of the group. If you prefer to see it all laid out, Figure 1 compares healing rates, and Figure 2 shows how the pain scores changed over time. The significant reduction in persistent rectal bleeding in Group A (3.3%) compared to Group B (30.0%) is summarized in Figure 3.

Table 1: Demographic Characteristics of Patients in the Research (n = 60)

Variable	Group A	Group B	P-value
Age (years)	44.0 ± 14.1	44.4 ± 13.9	0.91
Gender			
Male	19 (63.3%)	13 (43.3%)	0.12
Female	11 (36.7%)	17 (56.7%)	
History of Constipation			
Yes	18 (60.0%)	17 (56.7%)	0.79
No	12 (40.0%)	13 (43.3%)	

Table 2: Location of Anal Fissures

Location	Group A	Group B	Total n (%)
Anterior	10	13	23 (38.3%)
Posterior	4	5	9 (15.0%)
Lateral	5	5	10 (16.7%)
Multiple	11	7	18 (30.0%)

Table 3: Healing Outcomes at 6 Weeks

Outcome	Group A (Metronidazole + Diltiazem)	Group B (Diltiazem Alone)	P-value
Healed	26 (86.7%)	14 (46.7%)	0.001*
Not Healed	4 (13.3%)	16 (53.3%)	

Table 4: Mean VAS Pain Scores

Time Point	Group A (Mean ± SD)	Group B (Mean ± SD)	P-value
Baseline	8.37 ± 1.56	8.30 ± 1.39	0.86
At 6 Weeks	1.23 ± 1.63	2.73 ± 1.76	<0.001*

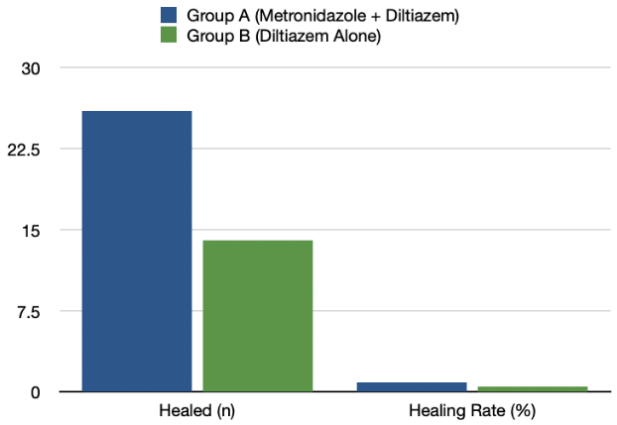

Figure 1: Healing Rates at 6 Weeks

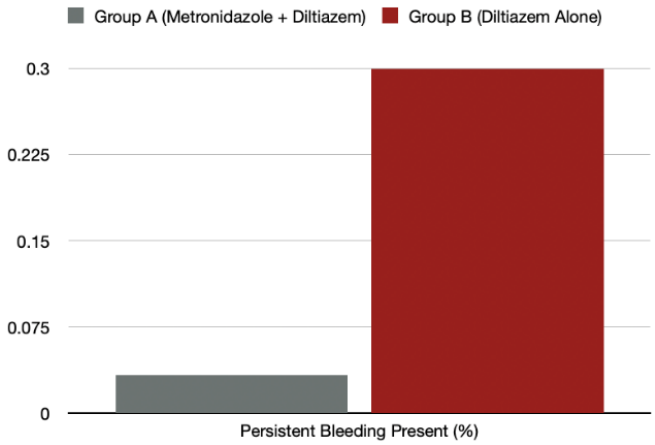

Figure 2: Reduction in VAS Pain Score

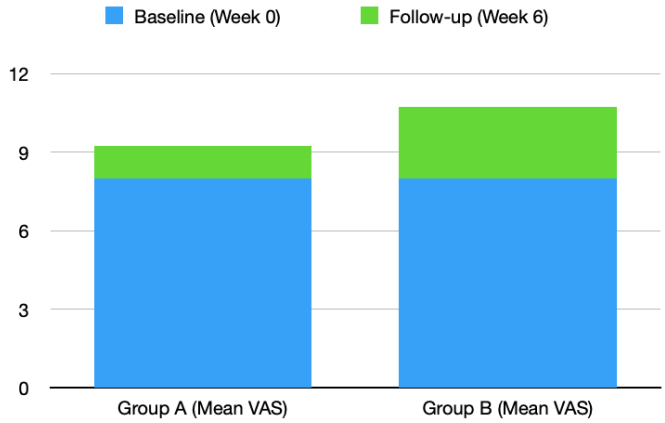

Figure 3: Rectal Bleeding at

Discussion

The results of this randomized controlled trial provide strong evidence for the dual-pathology hypothesis of acute anal fissure etiology. Although the classical management of AAF has been studied, this randomized controlled trial strongly supports the idea that acute anal fissures have two main causes. In traditional therapy, which aims to relax the sphincter to enhance blood flow, our findings indicate that it is also necessary to treat underlying infection and inflammation. This was due to an 86.7% healing rate with 1% Metronidazole and 2% Diltiazem, compared with 46.7% with Diltiazem alone (p = 0.001). These results suggest an absolute recovery improvement of approximately 40, which is a clinically significant improvement for prospective patients with ailing conditions. Similar evidence has been observed by Mert (2023), who found healing of the fissure in 82 people using combination therapy, and only 42 people receiving diltiazem alone. Such correspondence to the current study also supports the idea of the wider application of combination-based therapeutic approaches.[6] Similarly, Shahid et al. (2022) from Pakistan reported higher results when topical metronidazole was combined with glyceryl trinitrate (GTN). They reported a combined approach of 97.1% and a monotherapy rate of 85.2% for GTN.[9] The research shows that topical antibiotics improve wound healing, regardless of the antibiotics used in different studies. The anal canal normally contains E. coli and Bacteroides bacteria, which disrupt tissue repair when they are not properly controlled.

Gallo et al. (2024) proposed that anaerobic microorganisms establish a biofilm on unprotected crevice surfaces, which blocks keratinocyte movement while sustaining persistent localized inflammation.[13] The irritation from this inflammation creates a severe problem that prevents Diltiazem from relaxing the sphincter muscles. The bacterial infection resolved after Metronidazole treatment, and the inflammation that caused the muscle spasm also resolved. Diltiazem will act as a vasodilator because it will achieve its intended function as stated. The population who received the combined treatment had a significant reduction in pain since the VAS score, they had dropped to 1.23. The control group did not exhibit any change in the levels of pain, which remained to be 2.73. These combination therapies are clear on their component effects in showing the effectiveness. Our findings support those of Elgendy et al. (2024), who reported that patients achieved 96% recovery after using both antibiotics and vasodilators, despite clinical trials not showing such clear results. Focusing exclusively on GTN, they only saw an 86% rate. Nonetheless, the variation failed to reach statistical significance (p-value=0.08).[11] This variation can be explained by variations in the compounding formulations, patients' adherence to them, or the chronicity of the fissures. However, in our trial, the ineffectiveness of monotherapy in more than 50% of Group B patients

raises the concern that calcium channel blocker monotherapy has a well-established therapeutic ceiling effect in chronic refractory patients.[14]

Anatomically, the study population exhibited a higher percentage of anterior fissures (38.3%) and multiple fissures (30.0%) compared to Western standards. This non-standard distribution is probably the reflection of the food and lifestyle circumstances that are dominant in Azad Jammu Kashmir.[15] Traumatic defecation is one of the main causes since the constipation rate is high (51.7%). Anterior fissure is usually associated with multiparity and occult sphincter defects in women, whereas our data revealed anterior fissure in men. This implies that the etiology of our region may be strongly dependent on hard, abrasive stools rather than pure ischemic infarction; hence, the administration of antibiotics to prevent secondary infection of the traumatic wounds. It has serious clinical ramifications for resource-scarce environments such as Pakistan. Lateral Internal Sphincterotomy (LIS) is the best treatment for chronic fissure, but it has a risk of fecal incontinence between 3 and 45 percent. Al-Ubaide et al. (2022) observed that LIS is beneficial, but permanent changes in sphincter dynamics are possible, which makes conservative optimization the most important.[1] The surgeons can greatly reduce the surgical load and spare patients the risks of surgery by increasing the success rate of medical therapy, which now stands at around 47%. This study has some limitations.

The research results are limited in scope because the study included only 60 patients. The study took 6 weeks to complete, which made it difficult to study long-term symptom recurrence patterns. The researchers evaluated bacterial reduction using fissure-healing assessment because they did not perform microbiological tests. The study results have limited applicability because the researchers conducted their research at only one site. The study under consideration requires further research in different locations with the use of dominant laboratory analysis and additional microbiological examination to provide the researchers with more integrated information about the longitudinal impact endured by the participants.

Conclusion

The research proves that combined Metronidazole and Diltiazem therapy in acute treatment of anal fissures are more effective than other therapeutic interventions. Combination therapy was able to cure a very high healing rate of 86.7 per cent as equated to 46.7 per cent with Diltiazem monotherapy. When an antibiotic agent has been incorporated in the regular chemical sphincterotomy regime it shortens the healing period, lowers the pain, and increases control of hemorrhage. Safety of the patients was guaranteed and there was no increase in the number of adverse events as the combination regimen did not increase it. The evidence also contributes to the implementation of the Metronidazole Diltiazem therapy because it can be adopted as the treatment of choice of acute anal fissures, offering a more effective alternative to surgical intervention and, by extension, enhancing the overall patient outcomes and quality of life.

LIMITATIONS & RECOMMENDATIONS

There are a number of limitations that limit the analysis and the possible future applicability of the results. The strength of the applied research methodology, including random assignment to identify effective interventions and provide a clear meaning to the institutions that have to live with the limited state of resources, specific limitations deserve to be discussed. The independent variable was restrictive to one center and included a medium sample amount; and did not measure bacteria load reductions by the use of microbiological cultures. More than this, 6 weeks follow-up was not enough to estimate long-term outcome or recurrence. Future studies should counteract these shortcomings by incorporating multicenter studies, detailed bacteriological measurements, and follow up periods that are longer thus allowing these studies to deeply validate the findings. Improved therapeutic delivery processes can also reduce the need of a surgical intervention especially in environments where the health care resources are limited.

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