

A RANDOMIZED TRIAL OF TOPICAL DIAZEPAM AND TOPICAL DILTIAZEM IN THE TREATMENT OF CHRONIC ANAL FISSURE.

General Surgery

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ABSTRACT

Background: Anal fissure is a common surgical problem causing pain and discomfort in the perineal region. Surgery was the definitive treatment for chronic anal fissure but emerging non pharmacological therapy with diltiazem, nitroglycerine has made non surgical treatment the first choice in treating it. Although there are many advantages with non surgical therapy, surgical sphincterotomy is the ultimate treatment for fissure in ano and each method has its own disadvantages.

Aim: To determine and compare the outcome of topical diazepam and topical diltiazem in the treatment of chronic anal fissures

Objectives: To determine the efficacy of topical diazepam and topical diltiazem on chronic anal fissures by assessing pain relief and per rectal bleeding and to determine the side effects of diazepam and diltiazem on chronic anal fissure like faecal incontinence, perianal itching, dizziness.

Materials and methods: Around 60 patients presented to department of general surgery out patient department were included in sequential manner based on inclusion criteria. Clinical examination and history was obtained from these patients and 1 group of patients received Diltiazem cream and other group received Diazepam cream, both given in similar looking containers. These patient were reviewed 6 weeks after the therapy to look for reduction of symptoms and also to look for side effects.

Results: We have concluded that majority of the chronic anal fissure occur among male gender (61.66 %). This study also concludes that the maximal incidence of chronic anal fissure occurs in the middle aged group and that pain is the most common presenting complaint in chronic anal fissure. Pain relief and bleeding was better with 2% Diltiazem when compared with 2% Diazepam, and side effects were lesser in patients who used Diltiazem when compared with Diazepam (3 patients complained of dizziness).

Conclusion: Both diltiazem and diazepam has their own merits and demerits. In spite of many studies showing the superiority of diltiazem over other pharmacological preparations, in this study where diltiazem was compared with diazepam we conclude that diazepam is not efficacious than diltiazem. Larger study population and multicentric studies need to be done to concrete this evidence.

KEYWORDS

Anal fissure, Diltiazem, Diazepam

INTRODUCTION :

Chronic anal fissure is defined as symptomatic anal fissure without any relief for more than 6 weeks¹. Anal fissure is considered as one of the common causes of severe anal pain². Anal fissures are longitudinal or elliptical tears or ulcers in the distal anal canal, extending below the dentate line to the anal verge³. These lesions are typically seen by visual inspection of the anal verge. Anal fissure is often manifested by anal pain during defecation and also bleeding. Acute anal fissures often heal spontaneously or with conservative management namely high fiber diet, administration of stool softeners and warm sitz bath and do not require medical intervention. Chronic anal fissure, however, require medical intervention including surgical or chemical sphincterotomy⁴.

Diltiazem, a benzothiazepine-calcium channel blocker that is widely used in the therapy of hypertension and angina pectoris. It acts by decreasing the intracellular calcium which inhibits the contractile processes of the myocardial smooth muscle cells, causing dilatation of the coronary and systemic arteries.

Diazepam is a benzodiazepine. It acts centrally to relax smooth muscles⁵. Since diazepam is cheaper and has less side effects, local application of diazepam is being tried in the treatment of chronic anal fissure in this study.

The need for this study is to know the difference in the efficacy of topical diazepam and topical diltiazem in the treatment of primary chronic anal fissure.

AIMS AND OBJECTIVES:

AIM: To determine and compare the outcome of topical diazepam and topical diltiazem in the treatment of chronic anal fissures

OBJECTIVES:

To determine the efficacy of topical diazepam and topical diltiazem on chronic anal fissures by assessing pain relief and rectal bleeding.

To determine the side effects of diazepam and diltiazem on chronic anal fissure like dizziness, perianal itching, fecal incontinence.

SUBJECTS AND METHODS :

STUDY SUBJECTS :

This is a randomized control trial that was conducted in Mahatma Gandhi Medical College and research institute, a tertiary care hospital, between January 2018 – February 2020 after obtaining Institute Ethics Committee clearance. Around 50 patients who presented to the general surgery out patient department were enrolled in a sequential manner. Those patients who were above 18 years of age and having symptomatic anal fissure for more than 6 weeks were included in this study while pregnant women and patients with secondary anal fissure was excluded from this study.

METHODOLOGY :

A written and informed consent was obtained from each patient before recruitment to the study. On presentation the history of anal pain, per rectal bleeding, constipation, co-morbidities, use of other medications, history of similar episodes in the past and other relevant history was noted and a thorough clinical examination including per rectal and proctoscopic examination to know the position of anal fissure, skin tag & associated internal hemorrhoids was done.

Group (A) received 2% diltiazem and group (B) received 2% diazepam which was applied 3 times a day for 6 weeks. Patients were instructed to dispense a pea-sized amount of cream on their fingertip and apply a thin layer on their anoderm 3 times a day. They were reviewed weekly for the first 2 weeks and on sixth week.

Anal pain was measured using visual analogue scale (VAS). Both group of patients were reviewed for any side effects like perianal itching, fecal incontinence and dizziness in every visit.

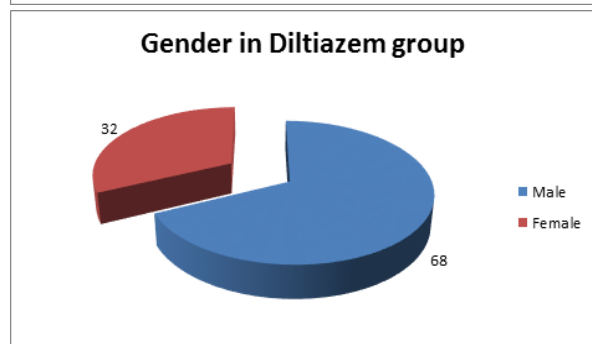
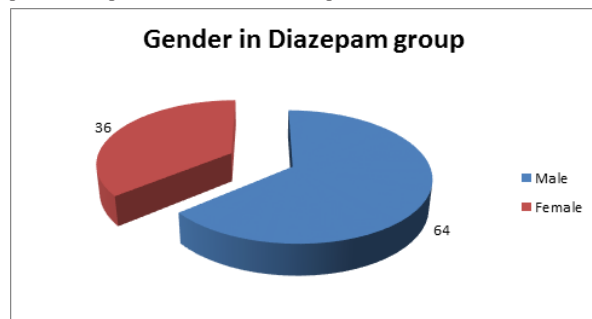
This study was terminated at the end of the study period or if the symptoms persist > 2 weeks. Statistical analysis was then calculated for

individual parameters using Mc Nemar test for the comparison of qualitative variables and chi-square test was calculated comparing two groups.

RESULTS :

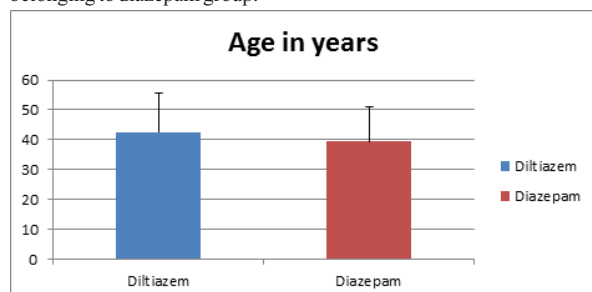
GENDER DISTRIBUTION :

This study shows that majority of the patients were male. Out of the 50 patients 33 patients were male and 17 patients were female



AGE DISTRIBUTION

Out of the 50 patients included in this study, mean age of patients in diltiazem group was 42.56 years and it was 39.48 years in patients belonging to diazepam group.

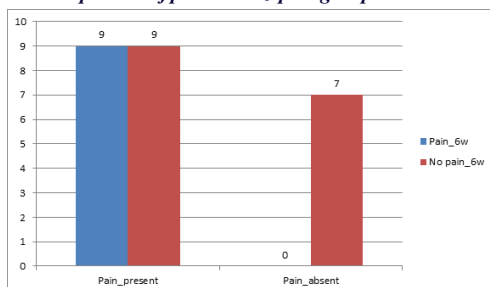


COMPARISON OF PAIN :

The table given below indicates that out of the 25 patients belonging to Diazepam group, pain was initially present in 18 patients. And after local therapy with diazepam at the end of 6 weeks there was no pain in 9 patients, while 9 subjects still complained of pain.

Diazepam	Pain At 6 weeks		Total	P value
Pre-treatment	Present	Absent		
Present	9	9	18	0.01
Absent	0	7	7	
Total	9	16	25	

Figure 8: Comparison of pain in diazepam group



In this table listed below, 20 subjects out of the total 25 patients belonging to diltiazem group had pain when they presented. But by the end of 6 weeks, only 3 had persistent pain and remaining 22 patients reported no pain.

Table 2: Comparison of pain in diltiazem group

Diltiazem	Pain At 6 weeks		Total	P value
Pre-treatment	Present	Absent		
Present	3	17	20	0.01
Absent	0	5	5	
Total	3	22	25	

COMPARISON OF BLEEDING

In this study, per rectal bleeding was compared among the two group who received diazepam and diltiazem. According to table no 3 and 4, totally 15 patients in Diazepam group and 13 patients from diltiazem group presented with bleeding initially. And by the end of the study period, 4 patients had persistent bleeding from diazepam group and only 1 patient had bleeding from diltiazem group.

Table 3: Comparison of bleeding in diazepam group

Diazepam	Bleeding At 6 weeks		Total	P value
Bleeding Pre-treatment	Present	Absent		
Present	4	11	15	0.01
Absent	0	10	10	
Total	4	21	25	

Table 4: Comparison of bleeding in diltiazem group

Diltiazem	Bleeding At 6 weeks		Total	P value
Bleeding Pre-treatment	Present	Absent		
Present	1	12	13	0.01
Absent	0	12	12	
Total	1	24	25	

COMPARISON OF ITCHING

According to the tables listed below, 8 patients in diazepam group had perianal itching on presentation out of the 25 patients. After 6 weeks 5 patients still complained of itching after using diazepam for 6 weeks.

Table 5: Comparison of itching in diazepam group

Diazepam	Itching At 6 weeks		Total	P value
Itching at Pre-treatment	Present	Absent		
Present	5	3	8	0.25
Absent	0	17	17	
Total	5	20	25	

Table 6: Comparison of itching in diltiazem group

Diltiazem	Itching At 6 weeks		Total	P value
Itching at Pre-treatment	Present	Absent		
Present	4	11	15	0.01
Absent	0	10	10	
Total	4	21	25	

The above table shows that 15 out of the 25 patients had itching on their first visit and after 6 weeks only 4 had itching.

DISCUSSION :

Anal fissure is a common anorectal problem that causes severe pain on defecation and also at rest. Surgical methods used in treating chronic anal fissure is highly efficient, but its associated with side effects like transient fecal incontinence which lead to the quest of non surgical management through chemical sphincterotomy using pharmacological agents⁵. Although medical therapy is less effective than surgical measures, it should be offered first because they are widely available, has good tolerance and associated with less severe complication⁶.

In this study comprising of 25 patients in each group, majority of them was male. In group A, 68 % of them were males and in group B 64 % of them were males. A similar study done by Khan et al in Pakistan also reported that males comprised of the majority in their study population. Various studies were done in the past which showed no significant difference in the gender predominance between diltiazem and other preparations^{7,8}.

In this study conducted, mean age of group A was 42.56 years and that of group B was 39.48 years. The age range of patients was 18-67 in this study. Ala et al in his study done at Iran comparing diltiazem and

captopril preparations, the mean age was 34.4 and 33.7 years in each group respectively and is similar to the current study. Khaledifar et al conducted a study comparing nifedipine and isosorbidedinitrate, where the mean age of two groups were 33.21 and 34.25 years. One more study done in Pakistan comparing two topical preparations on anal fissure showed a mean age of 43.84⁹. The above mentioned different studies done in various countries proved that mean age was almost similar to each other and the current study also has the same results. Thus based on the above mentioned studies chronic anal fissure is a disease of the middle aged population.

There is a significant decrease in pain after the study period for the group which used diltiazem when compared with glyceryl trinitrate⁹. Khan et al conducted this study and also reported better healing rates for the group which used diltiazem. Where as in the present study conducted, 20 patients (80%) of group A had pain on presentation and at the end of 6 weeks 3 of them had persistent pain. And the patients in group B who received diazepam topical preparation, 18(72%) had pain on presentation and after 6 weeks 9 patients had persistent pain. According to the study done by Hang et al where two different preparations of Diazepam was used, a significant reduction in pain and bleeding was noticed¹ among the 2 preparations. Similar randomised trial done in Karachi by Pradhan et al, comprised of 60 patients totally comparing Diltiazem and Glyceryltrinitrate. Patients who used the Diltiazem had better pain relief when compared to glyceryltrinitrate¹⁰. In this present study when anal bleeding was compared, 13 patients (52%) in group A and 15(60%) patients in group B initially had bleeding on initial presentation. And by the end of six weeks only 1 patient had complaints of bleeding from group A and in group B, 4 patients had persistent bleeding. Tomar and saxena who did their study in New delhi showed no significant decrease in the symptoms when diltiazem and glyceryltrinitrate was compared¹¹. An observational study by Knight et al¹² showed treatment with 2% topical diltiazem in 71 patients. It was observed that 75% experienced healing in 2 months and in further 2 months 88% experienced healing on using diltiazem. Minor side effects were perianal dermatitis and recurrent fissures. Another study by Jonas et al¹³ showed efficacy of diltiazem for chronic anal fissures that failed to heal with Glyceryl tri nitrate. In this study conducted 60 % had itching on presentation from group A whereas 32% had itching from group B. At the end of six weeks 4 patients from group A and 5 patients from group B had itching as their complaint which was present even after 6 weeks of treatment.

Griffin et al¹⁴ concluded in his study that topical 2% diltiazem is an effective and safe treatment for patients who fail topical 0.2% GTN. When the side effects of diltiazem and diazepam namely dizziness and incontinence was compared in the present study, it was found that none of the 60 patients experienced incontinence at the end of six weeks. And 3 patients belonging to the group B had complaints of dizziness at the end of six weeks.

Thus by this study, Diltiazem was more efficient than Diazepam in treating chronic anal fissures according to the number of patients who reported reduction of symptoms. This study also concludes that diltiazem reported in causing less side effects than diazepam.

LIMITATIONS:

Larger study with larger sample size is required to establish the efficacy and side effects of diazepam and diltiazem.

CONCLUSION:

Both diltiazem and diazepam have their own merits and demerits. In spite of many studies showing the superiority of diltiazem over other pharmacological preparations, in this study where diltiazem was compared with diazepam we conclude that diazepam is not efficacious than diltiazem. Larger study population and multicentric studies need to be done to concrete this evidence.

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