



## ROLE OF TOPICAL DIAZEPAM AND DILTIAZEM IN CHRONIC ANAL FISSURE - A REVIEW

### General Surgery

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### KEYWORDS

#### INTRODUCTION :

Chronic anal fissure is defined as symptomatic anal fissure without any relief for more than 6 weeks<sup>1</sup>. Anal fissures are considered one of the commonest causes of severe anal pain<sup>2</sup>. Anal fissures are longitudinal or elliptical tears or ulcers in the distal anal canal, extending below the dentate line to the anal verge<sup>3</sup>. 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 sphincterotomy<sup>4</sup>.

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 muscles<sup>1</sup>. 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.

#### METHODS:

Relevant publications collected from Pub Med , Google scholar, EMBASE, MEDLINE ,Cochrane database of systematic reviews were included in the review. The key search words used were anal fissure , diltiazem and diazepam .No restrictions were made based on date of publication. Duplicate copies of the publications were eliminated.

#### 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 agents<sup>5</sup>. 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 complication<sup>6</sup>.

One study done in Georgia in 2017, where 2 different preparations of diazepam was used to treat chronic anal fissure. This study was a single institution non experimental study , where patients over 18 years of age was included in study .The total sample size was 37. Primary end points were taken as reduction in pain and bleeding intensity .The study showed that overall mean age was 51 years ,pain was present in 36 patients and 33 patients had bleeding complaints .Finally this study concluded that diazepam is an effective and well tolerated treatment for chronic anal fissure<sup>1</sup>.

In a study done in Pakistan by Khan et al reported that males comprised of the majority in their study population. In this study he compared the efficacy of diltiazem and glyceryl trinitrate in chronic anal fissures and there is a significant decrease in pain after the study

period for the group which used diltiazem when compared with glyceryl trinitrate<sup>7</sup>.

Another study done in Medhi et al in Bangalore from 2009 to 2011, compares the effectiveness and side effects of 2% Diltiazem gel local application and internal sphincterotomy in the treatment of chronic fissure in ano<sup>3</sup>. The patients were divided into 2 groups, group A received Diltiazem cream for 6 consecutive weeks and group B patients underwent lateral internal sphincterotomy surgery. Group A patients were followed up weekly for 6 weeks on outpatient basis. Comparison between Group 1 and Group 2 did not show any difference in pain relief or fissure healing . Finally this study concluded that chemical sphincterotomy with Topical 2% Diltiazem should be the first option of treatment for chronic anal fissure. Internal sphincterotomy should be offered to patients with relapse and failure of prior pharmacological treatment<sup>3</sup>.

A study conducted in Ala et al in Iran in 2014, compared the effectiveness of topical diltiazem and topical captopril. It was a randomized controlled trial, total of 63 patients were included in the study and divided into 2 groups. There were no significant differences in bleeding or perianal irritation between the 2 groups, but the incidence of pruritus was higher in the captopril group, and at the end of the trial more than 45 % of the patients in this group still suffered from pruritus<sup>7</sup>. Topical captopril and diltiazem were found to be equally effective in the management of pain, bleeding and perianal irritation due to chronic anal fissure, but due to the high incidence of pruritus with topical captopril it is not recommended for the treatment of chronic anal fissure<sup>7</sup>.

Sajid et al conducted a similar study where analysis on investigating the effectiveness of diltiazem and glyceryltrinitrate for the nonsurgical management of chronic anal fissure was done. It included 481 patients. 238 patients were treated with diltiazem and 243 were given glyceryl tri nitrate. After analysing the results of all these studies, they came to a conclusion that both topical drugs are equally effective, but since diltiazem has fewer side effects when compared to glyceryl tri nitrate, it was concluded that diltiazem is the first line of conservative management in chronic anal fissure<sup>15</sup>.

Samim et al in his study, compared topical diltiazem cream with botulinum toxin injection in the treatment of chronic anal fissure. 134 patients were randomized to receive either diltiazem cream and placebo injection or BTA injection and placebo cream. The primary end point was fissure healing after 3 months. After 3 months, healing of the fissure was noted in 43% patients in the diltiazem group and 43% patients in the BTA group. Perianal itching was the only side effect and noted in 15% of patients in the diltiazem group, and this difference was statistically significant<sup>16</sup>. This study showed that there is no significant advantage of one treatment when compared to other.

Griffin et al did a study on 2% diltiazem . 47 patients who had previously failed treatment with glyceryl tri nitrate was taken as sample size from a single centre .Symptoms of pain bleeding and itching were recorded in sequential visits .This study concluded that topical 2% diltiazem is an effective and safe treatment for patients who fail topical 0.2% GTN<sup>14</sup>.

Another study by Jonas et al 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<sup>15</sup>.

Kocher et al this was a double blind randomized trial ,had 26 patients in each group compared adverse effects of glyceryl tri nitrate and diltiazem in the treatment of chronic anal fissure. Both creams were applied perianally for 6-8 weeks after obtaining consent There were increased side effects with Glyceryl tri nitrate .This study showed that there was no difference in healing rates when both preparations were compared but diltiazem therapy was shown to cause less headache than glyceryl trinitrate therapy<sup>18</sup>.

In observational study by Knight et al, diltiazem cream has been used as an alternative method to chemical sphincterotomy .This study showed treatment with 2% topical diltiazem in 71 patients. Study period was about 9 weeks .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<sup>12</sup> and no other side effects were noted .This study concluded that topical diltiazem for chronic anal fissure had significant healing rates and no significant side effects<sup>12</sup>.

Tomar and Saxena who did their study in New delhi, compared diltiazem and glyceryl tri nitrate preparations. Sample size was 50 divided into 2 groups .Group 1 received diltiazem and group 2 received glyceryl tri nitrate and followed up for 6 weeks .This study concluded that no significant decrease in the symptoms when diltiazem and glyceryltrinitrate was compared<sup>11</sup> but diltiazem was better tolerated and showed lesser side effects<sup>17</sup>.

Similar randomised trial done in Karachi by Pradhan et al in 2014, comprised of 60 patients totally comparing Diltiazem and Glyceryltrinitrate.Pain was measured using visual analogue scale and overall cost of treatment was also measured as a secondary outcome. It showed that majority of the patients belonged to male gender and overall mean age was 37 (11)years . Patients who used the Diltiazem had better pain relief when compared to glyceryltrinitrate<sup>10</sup> and concluded that chemical sphincterotomy with diltiazem was an effective first line treatment for chronic anal fissure.

## CONCLUSION :

Treatment of chronic anal fissures remains a challenge even today .Both diltiazem and diazepam has their own side effects .Diltiazem has been compared with other topical preparations and also with surgical therapy and established its efficacy . Larger study population and multi centric study may be required in establishing further efficacy of diltiazem over diazepam.

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