The Professional Medical Journal
www.theprofesional.com

DOI: 10.17957/TPMJ/17.3918

ORIGINAL PROF-3918

ANAL FISSURE;

COMPARISON OF EFFECTIVENESS OF 2% DILTIAZEM OINTMENT TO 0.2% GLYCERYL TRINITRATE OINTMENT IN TREATMENT

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Article received on:
04/03/2017
Accepted for publication:
15/07/2017
Received after proof reading:
08/09/2017

ABSTRACT… Objectives: To compare the effectiveness of 2% Diltiazem ointment with 0.2% Glyceryl trinitrate ointment. **Place & period:** The study was conducted in surgical units, Bahawal Vicotria Hospital, Bahawalpur, Pakistan from 01-01-2016 to 31-12-2016. **Material & Method:** In this prospective comparative study, 160 patients with anal fissure were equally &randomly divided in two group A (received 2%diltiazem ointment) & group B (received 0.2% Glyceryl trinitrate ointment). The ointment had to be applied to anal verge twice daily for 6-8 weeks. Assessment was done at 2nd, 4th & 6th weekends for fissure healing, pain relief & side effects. **Results:** Complete fissure healing was observed in 80%of patients in group A & 70% in group B ($P<0.15$). Pain response was good & was fairly similar in both the groups. Headache occurred in 5% in group A & 20% in group B ($P<0.002$). Mean time taken for healing of fissure in group A was 5.5 ± 0.28 weeks & in group B was 5.8 ± 0.32 weeks ($P< 0.237$). Recurrence rate was 7.5% in group A & 17.5% in group B. **Conclusion:** Topical Diltiazem is preferred to topical Glyceryl trinitrate in the treatment of acute & chronic fissure, because it is associated with a few side effects.

Key words: Fissure in Ano, Pain during Defecation, Constipation.

Article Citation: Bukhari ST, Atiq-ur-Rehman S, Abdullah MS, Bukhari ST, Iqbal J. Anal fissure; comparison of effectiveness of 2% diltiazem ointment to 0.2% glyceryl trinitrate ointment in treatment. Professional Med J 2017;24(9):1354-1359.
DOI: 10.17957/TPMJ/17.3918

INTRODUCTION

An anal fissure is painful tear or split in the mucosa of the distal anal canal extending from the anal verge proximally towards the dentate line. The exact cause of primary anal fissure is unknown, anal fissures arise from the trauma caused by the strained evacuation of a hard stool or, less commonly, from the repeated passage of diarrhea.[1] Important causes of secondary fissures include Crohn's disease, leukaemia, infections and squamous carcinoma.[2] The pathogenesis of fissure in ano is not yet fully explained, however, increased tone of internal anal sphincter and poor perfusion of anterior and posterior ano-derm have been implicated.[1] Anal fissure may be associated with indurated edges, sentinel piles and hypertrophied anal papilla.[2]

It usually in young and middle aged adults but may also occur infants, children and elderly and equally common in both sexes. Anterior fissure are more common in females than males. The commonly occurring symptom in anal fissure is pain during and after defecation, bleeding is also common but not inevitable. Examination may reveal breach in anal mucosa anteriorly or posteriorly, tenderness and sentinel piles. Anoscopic examination is usually impossible with acute anal fissure.[8]

Various agents' glyceryl trinitrate (GTN), botulinum toxin, nifedipine, diltiazem hydrochloride (DTZ) and bethanechol have been used in treatment of anal fissure.[3,5]

Glyceryl trinitrate is widely prescribed for treating anal fissure world wide, but various studies have shown that Diltiazem has fewer side effects than GTN and takes less time to heal anal fissure.[6,7] we have planned this study in order to compare the effectiveness of 2% diltiazem ointment to 0.2% glyceryl trinitrate ointment in treatment of anal

fissure to know which one is a better option, so that some practical recommendation could be made to enhance recovery in patients with anal fissure.

OBJECTIVES

To compare the effectiveness of 2% Diltiazem ointment with 0.2% Glyceryl trinitrate ointment.

OPERATIONAL DEFINITIONS

Effectiveness

The effectiveness will be measured with the quick relief of symptoms and side effects.

HYPOTHESIS

The 2% Diltiazem is more effective and has fewer side effects than 0.2 % GTN in healing anal fissure.

MATERIAL AND METHODS

Study Design

Comparative analytical therapeutic trial

Study Setting

Department of Surgery, Bahawal Victoria Hospital Bahawalpur

Study Duration

01-01-2016 to 31-12-2016

Sample Size

The calculated sample size with 10% of margin of error, 90 % power of study will be 160 patients and magnitude of fissure healing was observed in 71.87% of DTZ group & 68.23% of GTN group in 6 weeks.[7]

Sampling Technique

Non probability purposive sampling

SAMPLE SELECTION

Inclusion criteria

Patients of both gender of age 18 and above presenting with history of painful defecation, Perianal pruritis and bleeding per rectum. The diagnosis will be made on the basis of demonstration of breach in anal mucosa.

Exclusion criteria

Patients having one of the following criteria will be excluded from study.

- Specific local pathological conditions (crohn's disease, anal cancers, tuberculosis).
- Associated complaints (abscesses, fistula)
- Patients with previous perineal surgery
- Presumed or confirmed pregnancy or lactation.
- Allergy to Diltiazem or GTN.
- Chronic headaches.

Selection and Allocation

All the patients presenting to surgical out patient department fulfilling the inclusion criteria will be entered in the study after informed written consent. Case sheets of the selected patients will be screened for various variables such as: age and sex of the patients.

Group A will consist of 80 patients and will be treated with 2% Diltiazem ointment.

Group B will consist of 80 patients and will be treated with 0.2% GTN ointment.

Data Analysis

The efficacy will be compared with its corresponding values (relief of symptoms) the collected information will be entered in SPSS version 10.00 and arranged through it. Quantitative data including age will be presented in descriptive statistics including mean and standard deviation. Qualitative data including sex (male/ female) and relief of symptoms (yes or no) at six weeks will be described as frequency distribution tables (frequency and percentage) and compared using chi-square test. P-value of 0.05 or less was considered significant.

RESULT

A total of 160 patients were included in this study. Group A (2% DTZ) had 80 patients with 52 male and 28 females. Group B (0.2% GTN) included 80 patients with 46 male and 34 females. Male to female ratio in group A was 1.85:1 and in group B was 1.35:1. The age of the patients ranged from

20 to 51 years with mean age of 37.3 in group A while in group B patients age ranged from 21 to 50 years with mean age of 40.1years. Mean duration of symptoms in group A was 10±1.5 weeks while in group B it was 12±1.4 weeks.

All the patients of both groups presented with severe pain during defecation with a mean pain score of 9 (range 8-10) on verbal rating scale (VRS). Constipation was reported in 70(87.5%) patients in group A and 74(92.5%) patients in group B. Bleeding per rectum was reported by 56(70%) patients in group A and 60(75%) patients in group B. Anal pruritis was reported in 56(70%) patients in group A and 48(60%) patients in group B. Perianal discharge was present in 30(37.5%) patients in group A and 34(42.5%) patients in group B. Table-I.

Regarding site of fissure in our study posterior midline fissure was present in 86% patients in group A & 85% patients in group B. Anterior midline fissure was present in 10% patients in group A & 11% patients in group B while both anterior & posterior midline fissure was present in 4% patients in group A & group B. The proportion of participants experience headaches was 5% in group A and 20% for group B. Other side effects observed in the two groups are shown in Table-II.

After 6 weeks of treatment, 85% of the study population showed excellent response in their symptoms in group A while in group B 75% study population showed excellent response. The mean pain score dropped from 9 to 2 in patients who were prescribed 2% DTZ group A whereas amongst those who applied 0.2% GTN group B, it fell from 9 to 3. Out of 80 patients in group A, 80% showed complete healing of fissure while in group B 70% patients showed complete healing of fissure. Table-III. Remaining patients in both groups showed partial response to treatment. The difference in healing observed between the two groups was statistically significant (Fisher exact=0.2009chi-square=0.2016, p=0.1503).

Following the completion of 8 weeks of treatment, patients were evaluated for recurrence of fissure. Recurrence rate was 7.5% in group A & 17.5% in group B.

	Group A	Group B
Age mean (range) years	37.3 (20-51)	40.1 (21-50)
Gender (Male : Female)	1.85:1	1.35:1
Mean symptoms Duration (weeks)	10±1.5	12±1.4
Painful defecation	80(100%)	80(100%)
Constipation	70(87.5%)	74(92.5%)
Bleeding per rectum	56(70%)	60(75%)
Anal pruritis	56(70%)	48(60%)
Perianal Discharge	30(37.5%)	34(42.5%)

Table-I. Patients demographic and symptoms profile. Group A (n=80) Group B (n=80)

Side effects	Group A (n=80)	Group B (n=80)	p-value
Headaches	4 (5%)	16(20%)	< 0.002
Vertigo	1 (1.25%)	5 (6.25%)	<0.059
Perianal itching	4 (10.0%)	3 (7.5%)	<0.36
Incontinence (flatus)	0 (0%)	1 (1.25%)	<0.25
Postural hypotension	4(5%)	10(12.5)	<0.051

Table-II. Side-effects during the treatment period

	Group A (n=80)	Group B (n=80)	P value
Mean time taken for decrease in symptoms (week).	2.6±0.25	2.8±0.30	0.107
Mean time taken for complete relieve of symptoms (week)	4.3±0.35	4.6±0.33	0.602
Complete relieve of symptoms (no of patients)	68(85%)	60(75%)	0.12
Fissure healing in no patients	64(80%)	56(70%)	0.15
Mean time taken for fissure healing in weeks	5.5±0.28	5.8±0.32	0.237

Table-III. Comparison of features of patients in both groups during follow-up

DISCUSSION

Fissure in ano is a common disease in this region. Patients usually present with pain, constipation & bleeding.[1,3] In our study the disease was in third & fourth decade of life, there was male predominance. These features were similar to previous studies.[2,3,4] In these study 100% patients in both groups presented with pain during or after defecation. Constipation was reported in 87.5% patients in group A & 92.5% patients in group B. Bleeding per rectum was reported in 70% patients in group A while in group B it was reported in 75% patients. Anal pruritis was reported in 70% patients in group A & 60% patients in group B. Perianal discharge was reported in 37.5% patients in group A & 42.5% patients group B. Painful defecation was the commonest symptom followed by constipation, anal pruritis & bleeding per rectum in literature.[6,7,8]

Regarding site of fissure in our study posterior midline fissure was present in 86% patients in group A & 85% patients in group B. Anterior midline fissure was present in 10% patients in group A & 11% patients in group B while both anterior & posterior midline fissure was present in 4% patients in group A & group B. Fissure in posterior midline was common than in the anterior midline in different studies.[5,7] Clinical evaluation revealed the presence of sentinel tag in 60(75%) patients in group A and 68(85%) patients in group B.

The treatment of anal fissure has shifted from surgical to medical modalities because of the risk of incontinence associated with surgery.[6,8] Chemical sphincterotomy can be done using a variety of agents. A first line use of medical therapy cures most anal fissures economically and conveniently.[7,9] Glyceryl trinitrate remains the standard chemical sphincterotomy. However, side-effects such as headaches and dizziness are common with nitrates, which may limit their application and reduce patient compliance.[9,10,11] In our study headache was noticed by 5% patients in group A & 20% patients in group B. vertigo was noticed by 1.25% patients in group A while in group B it was noticed in 6.25% patients. Perianal itching was noticed by 5% patients in group A while in group B it was noticed in 3.75% patients. Flatus incontinence was not noticed in group A patients while in group B it was noticed in 1.25%. In the present study, one patient developed flatus incontinence with the use of GTN ointment but it was reversible after cessation of treatment. Topical diltiazem is associated with fewer side-effects, probably because of minimal systemic absorption.[11,12] Studies also showed that topical diltiazem is an effective and safe treatment for chronic anal fissure in patients who have failed topical 0.2% GTN and need for sphincterotomy can be avoided in upto 70% of cases.[13] While it will be necessary to determine the outcome after a long period, the study has proved the superiority of diltiazem over glyceryl trinitrate in the short-term.[12,14,15] Postural hypotension was noticed in 5% patients in group A while in group B it was noticed in 12.5% patients.

This study has shown same rates of healing for both topical GTN and DTZ with no significant difference between them. Controlled clinical trials have shown varied results of healing (45-80%) with topical GTN.[9,10,12] & (60-85%) with topical DTZ.[14,15,16] In our study 85% patients of group A and 75% patients of group B has complete relieved of their symptoms. There was marked relieved of pain after using DTZ & GTN ointment by Behnam Sanei.[4] While Mean time taken for decrease in symptoms in group A was 2.6±0.25 weeks & in group B was 2.9±0.30 weeks. Mean time taken for complete relieves of symptoms in group A was 4.3±0.35 weeks & in group B was 4.6±0.33 week. Mean time taken for healing of fissure in group A was 5.5±0.28 weeks & in group B was 5.8±0.32 weeks. Complete healing of fissure in 80% of group A 70% of group B patients.

It was found that the combined effect of GTN and DTZ was greater than the effect of either agent alone.[4] Headache is a major problem for patients with anal fissure treated by GTN ointment.[9,10,12] Headaches were not reported in some initial studies using DTZ but neither were they reported in the initial case series using nitrates, and only became apparent in later trials.[16,17,18] Nevertheless, the number of headaches reported in this study were significantly fewer than with the GTN group.

In this study following the completion of 6 weeks of treatment, patients were evaluated for recurrence of fissure. Recurrence rate was 7.5% in DTZ & 17.5% in GTN group. Patients who had partial response or failed to show signs of healing and those who suffered from recurrence were offered proceeding to lateral internal sphincterotomy.[2,8,19]

CONCLUSION

Topical 2% diltiazem appeared to be well tolerated and equally effective first-line method of chemical sphincterotomy for both acute & chronic anal fissures. Long-term follow-up is needed to assess the risk of fissure recurrence after initial healing with diltiazem.

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"Inside every person you know, there's a person you don't know."

Unknown

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Syeda Tooba Bukhari	Collected the data of patient. Prapare the result	
2	Sheikh Atiq-ur-Rehman	Prapare the result, Discussion, Reivew of literature	
3	M. Shoaib Abdullah	Review of literature of Materials & Methods	
4	Syed Talha Bukhari	Review of literature of collected references	
5	Javid Iqbal	He helped in overall preparation, writing of article, conclusion of study.	