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Original Research Article

Evaluation of role of topical 0.2% Glyceryl trinitrate ointment and topical 2% Diltiazem ointment in healing of anal fissure

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Abstract

Backround: The patho-physiology of anal fissure is thought to be related to trauma to the anoderm from any cause. A tear in the anoderm causes acute pain, which results in spasm of the internal anal sphincter and decreased blood supply to the anoderm.

Aim: To comparative evaluation of topical 0.2% Glyceryl trinitrate ointment and topical 2% Diltiazem ointment in anal fissure and to evaluate the role of topical 0.2% Glyceryl trinitrate ointment and topical 2% Diltiazem ointment in healing of anal fissure as compared to prevalent conservative treatment i.e. topical anaesthetics.

Material and methods: The study was conducted on the patients of anal fissure reported in outpatient department of General Surgery at Guru Gobind Singh Medical College and Hospital, Faridkot including 60 patients which randomized in 3 groups, group A, group B and group C. The data was statistically analyzed using the SPSS version 16.

Results: Improvement in constipation after 8 weeks of treatment were 85%, 85% and 80% in Group A, B and C respectively and p value was non-significant (0.887). Improvement in bleeding after 8

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weeks of treatment were 90%, 90% and 85% in Group A, B and C respectively and p value was non-significant (0.851). Healing was 78.57%, 92.31% and 46.15% in Group A, B and C respectively.

Conclusion: Topical 2% Diltiazem and 0.2% Glyceryl trinitrate ointment are equally effective in healing of chronic anal fissure. However, early pain improvement and fewer side effect profile of Topical 2% Diltiazem ointment; this study suggests it as first line treatment of chronic anal fissure.

Key words

Glyceryl trinitrate, Diltiazem, Anal fissure.

Introduction

An anal fissure is a longitudinal split in the anoderm of the distal anal canal which extends from the anal verge proximally towards, but not beyond, the dentate line [1]. Patients of anal fissure present with symptoms of pain before and after defecation, constipation, and bleeding per rectum. On examination, intense spasm of sphincters is predominant feature but a skin tag may or may not be present. In pathophysiology of anal fissure, there is role of internal anal sphincter hypertonia and local ischemia [2, 3]. Anal fissures are categorises primary fissure and Secondary fissures. Primary fissure is a benign superficial ulcer in anal canal. It may be due to hard bulky stools. It may be of acute or chronic onset [4]. Acute primary anal fissure is superficial, with base formed by loose connective tissue; the transverse fibres of internal sphincter are not usually seen [5]. If the symptoms persist for >6-8 weeks, it is called chronic anal fissure [5].

Secondary anal fissure are those that arise in association with some other pathology e.g. Crohn's disease, anal TB, AIDS or a previous anal operation, syphilis, leucoplakia, leukemia and anal malignancy. Anal fissure may occur in any age group, but are most common in 2nd and 3rd decade of life [5]. Mostly, fissures occur posteriorly and but in females, it is more common anteriorly.

Nearly 90% of acute anal fissures will heal using conservative measures alone [6]. But only 20-30% chronic fissures are likely to heal by conservative measures. In the present study, we are comparing the efficacy of topical 2% Diltiazem ointment and topical 0.2% Nitroglycerine ointment. Aims and objectives of the study is comparative evaluation of topical 0.2% Glyceryl trinitrate ointment v/s topical 2% Diltiazem ointment in anal fissure and to evaluate the role of topical 0.2% Glyceryl trinitrate ointment and topical 2% Diltiazem ointment in healing of anal fissure as compared to prevalent conservative treatment i.e. topical anaesthetics.

Material and methods

Total 60 patients of anal fissure reported in outpatient department of General Surgery at Guru Gobind Singh Medical College and Hospital, Faridkot were selected for the study. These patients were randomly divided in 3 groups, group A, group B and group C. Each group contained 20 patients. Topical 0.2% Glyceryl trinitrate ointment was applied to 20 patients of Group A, Topical 2% Diltiazem ointment was applied to 20 patients of group B and group C was control group without any additional treatment. Patients with primary acute and primary chronic anal fissures were included in the study and patient with known hypersensitivity to topical Glyceryl trinitrate and

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Diltiazem, secondary chronic anal fissure, systemic diseases (Cardiac conduction defects, Sick sinus syndrome, acute MI, severe hypotension) and chronic headaches, in which Glyceryl trinitrate and Diltiazem are contraindicated, specific local pathological conditions, e.g., inflammatory bowel disease, anal cancer, tuberculosis, pregnancy or lactation, and patients having any concomitant skin disease in perianal region were excluded from the study.

Detailed history, investigations and assessment of lesions were recorded. Patients were explained about the procedure and an informed consent was taken. Before application, the site involved was cleaned with plain water, topical 0.2% Glyceryl trinitrate ointment or topical 2% Diltiazem ointment was gently pushed in the anus with a clean index finger/strip available with the preparation. After confirming the diagnosis by detailed history and clinical examination, topical 0.2% Glyceryl trinitrate ointment was applied twice a day or topical 2% Diltiazem ointment was applied three times a day. Both ointments were applied preferably after passing stools, including bed time application, for 8 weeks. First follow up visit was after 24 hours of first application to see any side effects e.g. erythema, edema, and pain. Next follow up visits was every week for 4 weeks, and then every two weeks for another 4 weeks, with a total of 7 follow up visits. Any untoward side effect was recorded during follow up period. Any patient with severe reaction discontinued. At every follow up visit response to treatment was recorded.

Results

Mean age for anal fissure in Group A, B and C were 38.35, 40.25 and 44.48 year respectivly. Range of age in Group A, B and C were 25-60, 27-70 and 20-74 years respectivly. Mean age and range for presentation in 60 patient was 41.15 and 20-74. Incidence of anal fissure was 36.66% in males and 63.33% in females, with ratio of 1: 1.7. Incidence of acute anal fissure was 40% and chronic fissure was 60%. P value was insignificant. Incidence of anterior anal fissure was 15% and posterior anal fissure was 85%. P value was 0.866 which was insignificant. Visual analogue scale was used for pain (0-10). At 24 hours, pain range in group A, B and C were 4-10, 5-10 and 6-10 ($P > 0.05$), at 1 week, pain range in Group A, B and C were 3-9, 2-9 and 5-9 ($P = 0.003$ between group B and C) as per **Table - 1**. At 2 week, pain range in group A, B and C was 3-9, 0-9 and 2-8 ($P = 0.003$ between group B and C). At 3 week, pain range in group A, B and C was 2-9, 0-9 and 1-7 ($P = 0.003$ between group B and C). At 4 week, pain range in group A, B and C was 0-8, 0-8 and 1-7 ($P = 0.007$ between group B and C). At 6 week, pain range in group A, B and C were 0-8, 0-8 and 0-8 ($P = 0.007$ between group B and C). At 8 week, pain range in Group A, B and C were 0-8, 0-8 and 0-8 ($P = 0.026$ between group B and C). Improvement in constipation between the three groups is insignificant at follow up as per **Table - 2**. Improvement in bleeding between all the three groups is insignificant at follow up as per **Table - 3**. Distribution of patients according to healing of fissure at 8 weeks showed that A vs. B: $x^2 = 0.625$; $df = 1$; $p = 0.429$; insignificant, A vs. C: $x^2 = 3.750$; $df = 1$; $p = 0.053$; insignificant, B vs. C: $x^2 = 7.033$; $df = 1$; $p = 0.008$; significant as per **Table - 4**. Distribution of patients according to healing of both acute and chronic fissure showed that in acute, A vs. B: $x^2 = 0.034$; $df = 1$; $p = 0.853$; insignificant, A vs. C: $x^2 = 0.034$; $df = 1$; $p = 0.853$; insignificant, B vs. C: $x^2 = 0.00$; $df = 1$; $p = 1.000$; insignificant and in chronic, A vs. B: $x^2 = 1.008$; $df = 1$; $p = 0.315$; insignificant, A vs. C: $x^2 = 6.238$; $df = 1$; $p = 0.013$; significant, B vs. C: $x^2 = 10.400$; $df = 1$; $p = 0.001$; significant as per **Table - 5**. 10% of group A patients had headache and no other

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adverse effects. Group B and C patients had no adverse effects as per **Table - 6**.

Discussion

Anal fissure is a very common problem across the world. It causes considerable morbidity and adversely affects the quality of life, and therefore appropriate treatment is mandatory. Traditionally, surgical treatments such as manual anal dilatation and an internal closed sphincterotomy have been used for this ailment [7]. Because of the disability associated with surgery for anal fissure and the risk of incontinence, medical alternatives for surgery have thus been sought. Pharmacologic methods that relax the anal sphincters, to accomplish reversibly what occurs in surgery, have been used to obtain fissure healing. K. Bielecki and M. Kolodziejczak in 2002 concluded from his study of 43 patients that the age of patients varied from 20 to 76 years with mean of 49.1 years [8]. Marion Jonas in 2002 reported that mean age was 42 years (range 20-80) [9]. McDonald, et al. in 1983, concluded in his studies that mean age was 39 years and range was 17-74 years [10]. In present study, mean age of anal fissure was 41 years with range 20-74 years. K. Bielecki and M. Kolodziejczak in 2002 concluded from his study of 43 patients that 12.5% were males and 87.5% were females. The male female ratio was 1: 7 [8]. Marion Jonas in 2002 reported that males were 33.33% and female were 66.67% [9]. In present study, the incidence of anal fissure is 36.66% in males and 63.33% in females, with ratio of 1:1.7 and p value was 0.789 (insignificant).

In one of the study in 2009, H M Abd Elhady, et al. published, the incidence of anal fissure in 160 patients were 80.63%, 11.25% and 8.13% in posterior, anterior and combined respectively [11]. In 2002, Marion Jonas reported, incidence of posterior anal fissure was 54%, anterior 44% and combined 2.5% [9]. K. Bielecki and M. Kolodziejczak in 2002 concluded that mostly anal fissure occurred posteriorly (95%) and in only 5% was anterior [8]. In present study, incidence of posterior anal fissure was 85% and anterior was 15%.In one of the study of 60 patients conducted by U.K. Shrivastava in 2007, mean pain score after 6 weeks in group A, B and C were 2, 3 and 5 respectively [12]. In present study, group A, B and C had mean pain score 2, 1 and 4 respectively.

In one of the study in 2009, Hamdy Abd Elhady, et al. published that 77% of group A and 70% of group B patient were pain free after 2 weeks of treatment with 0.2 % Glyceryl trinitrate and 2% Diltiazem ointment [11]. In present study, only 10% of group B patient were pain free. But after treatment for 8 weeks, the group A (40%), B (70%) and C (20%) were pain free.

In present study, improvement in constipation after 8 weeks of treatment were 85%, 85% and 80% in group A, B and C respectively and p value was non-significant (0.887) when we compare all the three groups.

In present study, improvement in bleeding after 8 weeks of treatment were 90%, 90% and 85% in group A, B and C respectively and p value was non-significant (0.851) when we compare all the three groups. Hamdy Abd Elhady, et al. conducted study of 160 patients in 2009, founded headache as adverse effect in 15% of Group A patient and 5% in Group B [11]. U.K. Shrivastava, et al. in 2007 reported, headache as adverse effects in 67% of patient treated with 0.2% glyceryl trinitrate (GTN) ointment and no adverse effects in group treated with 2% diltiazem ointment [12]. K. Bielecki and M. Kolodziejczak in 2002 conducted study of 43 patients comparing 0.2% glyceryl trinitrate (GTN) ointment and 2% diltiazem (DTZ) ointment. In

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their study headache reported only in group treated with 0.2% glyceryl trinitrate (GTN) ointment (33.33%) [8]. H.M. Kocher, et al. in their study in 2002, reported headache occurred in 17 (58.62%) of 29 patient in the GTN group, compared with 8 (25.81%) of 31 in the DTZ group [13]. In present study, headache was seen only in group A (10%).

One another study in 2009, Hamdy Abd Elhady, et al. published that healing percentage of GTN group was 86.5% and DTZ group is 80% [11]. Behnam Sanei, et al. in 2009 had conducted a randomized clinical trial of 102 and reported healing percentage of GTN group was 66.7% and DTZ group is 54.9% [14]. U.K. Shrivastava, et al. in 2007 concluded complete healing was observed in 73%, 80% and 33% patients in groups A, B and C respectively [12]. K. Bielecki and M. Kolodziejczak in 2002 concluded from his study of 43 patients that anal fissure had healed in 85.7% (group A) and 90% (group B) [8]. H.M. Kocher, et al. in their study in 2002, reported 86.2% in GTN group and 86.2% in DTZ group [13]. In present study, healing was 78.57%, 92.31% and 46.15% in group A, B and C respectively. A study done by Hasegawa H, et al., in 2000, reported healing percentage in GTN group was 81% [15]. In present study, healing percentage of acute anal fissure in group A, B and C was 60%, 71.43% and 71.43% respectively.

Conclusion

It is concluded from the present study that Incidence of anal fissure was more in middle age group i.e. in four ties. Females were more commonly affected than males in ratio of 1.7: 1. Posterior fissures were more common than anterior in ratio of 5.6: 1. Pain improvement was significant between Diltiazem vs. control groups. Improvement in constipation and bleeding per rectum was insignificant between the groups. Acute anal fissure was healed non-significantly in all the three groups. Chronic anal fissure was healed significantly between study groups and control group but on significant healing between study groups. Adverse effect i.e. headache was only found in GTN Group. Dermatitis and other adverse effects were not found in any group. This study showed that topical 2% Diltiazem and 0.2% Glyceryl trinitrate ointment were equally effective in healing chronic anal fissure. However, early pain improvement and fewer side effect profile of Topical 2% Diltiazem ointment; this study suggests it as first line treatment of chronic anal fissure.

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Table – 1: Distribution of patients according to improvement in pain.

Time interval	Pain (mean score)			Significance (p value)		
	Group A	Group B	Group C	A vs B	A vs C	B vs C
Pre-Treatment	8.45 ± 1.79	8.40 ± 1.39	8.45 ± 1.28	-	-	-
24 hours	8.45 ± 1.79	8.40 ± 1.39	8.45 ± 1.28	0.994	1.00	0.994
1 week	6.35 ± 1.57	5.35 ± 2.03	7.10 ± 1.17	0.136	0.319	0.003*
2 weeks	5.25 ± 1.55	3.95 ± 2.37	5.95 ± 1.32	0.067	0.443	0.003*
3 weeks	4.40 ± 1.76	3.20 ± 2.63	5.45 ± 1.61	0.162	0.245	0.003*
4weeks	3.40 ± 2.30	2.15 ± 2.35	4.45 ± 2.28	0.210	0.329	0.007*
6 weeks	2.40 ± 2.42	1.40 ± 2.28	3.85 ± 2.66	0.408	0.158	0.007*
8 weeks	1.95 ± 2.69	1.20 ± 2.59	3.50 ± 2.88	0.660	0.178	0.026*
* $p < 0.05$; Significant						

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Table – 2: Distribution of patients according to constipation.

Time interval	No. of patients			p value
	Group A	Group B	Group C	
Pre-treatment	17	16	16	-
24 hours	17	16	16	0.895^{NS}
1 week	5	5	7	0.720^{NS}
2 weeks	5	5	6	0.918^{NS}
3 weeks	4	4	6	0.689^{NS}
4weeks	2	2	4	0.562^{NS}
6 weeks	2	2	2	1.000^{NS}
8 weeks	3	3	4	0.887^{NS}

(NS = Not Significant)

Table – 3: Distribution of patients according to bleeding per rectum.

Time interval	No. of patients			p value
	Group A	Group B	Group C	
Pre – treatment	17	16	16	-
24 hours	17	16	16	0.895^{NS}
1 week	12	7	9	0.280^{NS}
2 weeks	5	3	5	0.675^{NS}
3 weeks	3	2	4	0.676^{NS}
4weeks	1	1	3	0.418^{NS}
6 weeks	1	1	3	0.418^{NS}
8 weeks	2	2	3	0.851^{NS}

(NS = Not Significant)

Table – 4: Distribution of patients according to healing of fissure at 8 weeks.

Healing at 8 weeks	Group A		Group B		Group C	
	No.	%	No.	%	No.	%
Complete	15	75	17	85	09	45
Not complete	5	25	3	15	11	55
Total	20	100	20	100	20	100

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Table – 5: Distribution of patients according to healing of both acute and chronic fissure.

Duration of fissure	No. of patients (%) having complete healing at 8 weeks		
	Group A	Group B	Group C
Acute	60	71.43	71.43
Chronic	78.57	92.31	46.15

Table – 6: Distribution of patients according to adverse effects.

Adverse effects	Group A		Group B		Group C		p value
	No.	%	No.	%	No.	%	
Headache	2	10	0	0	0	0	0.126
Dermatitis	0	0	0	0	0	0	
Total	20	100	20	100	20	100	

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