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To Compare the Effectiveness of Topical Application Of 2% Diltiazem Versus 2% Lignocaine in the Treatment of Chronic Fissure in Ano

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I. INTRODUCTION

An anal fissure is a linear ulcer usually found in the midline, distal to the dentate line.[1] Anal fissure most often is manifested with excruciating anal pain (because of its location extending onto the very sensitive anoderm) with defecation and bleeding.

A tear in the anoderm causes spasm of the internal anal sphincter, which results in pain, increased tearing, and decreased blood supply to the anoderm. This cycle of pain, spasm, and ischemia contributes to development of a poorly healing wound that becomes a chronic fissure.[2]

An acute fissure is a superficial tear of the distal anoderm. Chronic fissures develop ulceration and heaped-up edges. There is often an associated external skin tag and/or a hypertrophied anal papilla internally.

A chronic fissure, with more than 6 weeks of symptoms, is usually deeper and generally has exposed internal sphincter fibers in its base. It is frequently associated with a hypertrophic anal papilla at its upper aspect and sentinel pile at its distal aspect. Based on etiology it is classified as primary (idiopathic) or secondary. Secondary fissures are those that occur due to some other pathology such as Crohn's disease, anal tuberculosis, AIDS. Patients usually present with pain during defecation and passage of bright red blood per anus.

The precise etiology of anal fissure is unknown. Fissure is most commonly attributed to trauma from the passage of a large hard stool. Painful fissures are generally associated with involuntary spasm of the internal sphincter with high resting pressure in the anal canal. Reduction of anal sphincter spasm results in improved blood supply and healing of fissure.

Surgical techniques like manual anal dilatation or lateral internal sphincterotomy, effectively heal most fissures within a few weeks, but may result in permanently impaired anal continence. This has led to the research for alternative non-surgical treatment like nitrates,calcium channel blockers (nifedipine,diltiazem) have been shown to lower resting anal pressure and heal fissures without threatening anal continence .

The present study compares the effectiveness and side effects of 2% Diltiazem gel local application and lignocaine in the treatment of chronic fissure in ano

Aim and Objectives of the study

1. To compare the effectiveness of topical application of 2% diltiazem versus 2% lignocaine in the treatment of chronic fissure in ano

II. MATERIALS AND METHODS

Study design:Prospective study
Study setting:Chettinad hospital and research institute.
Study period:18 months(Jan 2021 –Jun 2022)
Study population: All patients fullfilling the inclusion criteria with definitive diagnosis of chronic fissure in ano during the study period.
Sampling method: Purposive sampling method.
Sample size:60 cases in each group.

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Inclusion Criteria:

- Patients with confirmed diagnosis of chronic fissure in ano
- Patients age ranging from 18 to 60 years of age of both sexes.
- Patients willing to be part of the present study.

Exclusion Criteria:

- Pregnant women with fissure in ano.
- Patients with cardiac disease,hypertension.
- Fissures associated with hemorrhoids,fistula,malignancies.
- Fissures secondary to specific diseases like Tuberculosis,Crohn's disease.

Tools to be used in the study:
Digital rectal examintion, proctoscopy were done in all patients giving consent for the present study.
Special investigations done if required- Sigmoidoscopy, colonoscopy, stool examination, examination of discharge from anal fissure, VDRL ,biopsy.

Procedure for data collection:

All patients presenting with symptoms of anal fissure was examined thoroughly and a detailed history was taken as per the proforma. The patients were finalized for the present study as per the inclusion and exclusion criteria.consent is taken.

Digital rectal examination done to assess the extent and the degree of the anal fissure. Proctoscopic examination done in all patients and the findings was noted down.

In this prospective study ,patients with fissure in a Ano are divided in two groups. Both groups are adviced to take high fibre diet,sitz bath,laxative lactulose syrup two teaspoons at bed time.

Group 1 are advised to apply 2% Diltiazem and group 2 are advised to apply 2% lignocaine twice daily for 6 weeks. Patients were instructed to apply the gel(about size of a pea) atleast 1.5 cm to 2 cm into the anus twice daily for 6 consecutive weeks. Patients were advised to wash the hands before and after use of gel.

Statistical Analysis of data:

The data will be entered into MS Excel 2007 version and further analyzed using SPSS 20.
For descriptive analysis, the categorical variables was analyzed by using percentages and the continuous variables were analyzed by calculating mean ± Standard Deviation.

For inferential analysis, The numerical data were analyzed using "t test" test , The categorical data were analyzed using Chi square test. was applied and "p" <0.05 was considered as statistically significant

III. RESULTS

Table 1: Age distribution

	2% diltiazem		2% Lignocaine		Total	
	N	%	N	%	N	%
<40 years	16	53.3%	18	60%	34	56.7%
>40 years	14	46.7%	12	40%	26	43.3%
Total	30	100.0%	30	100.0%	60	100%
Mean ± SD	42.03 ± 17.46		38.50 ± 10.87		40.26 ± 14.53	
Chi square test = 0.26, p=0.60 , Not statistically significant						

In the present study the mean age of the study participants in conservative group was 42.03 ± 17.46 and 2% Lignocaine was 38.50 ± 10.87.
53.3% were in <40 years group and 46.7% were >40 years in the conservative group.

In the 2% Lignocaine, 60% were in <40 year and 40% were >40 year.
There was no statistically significant association observed between two groups with relation to age as the p value calculated to be >0.05.

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Table 2: Gender distribution

	2% diltiazem		2% Lignocaine		Total	
	N	%	N	%	N	%
Male	20	66.7%	15	50.0%	35	58.3%
Female	10	33.3%	15	50.0%	25	41.7%
Total	30	100.0%	30	100.0%	60	100%
Chi square test = 1.68 , p=0.19 , Not statistically significant						

Distribution based on gender shows in the Diltiazem group 66.7% were male and 33.3% were female.
In the 2% Lignocaine, 50% were male and 50% female.

There was no statistically significant association observed between two groups with relation to gender as the p value calculated to be >0.05.

Table 3: Age and Gender distribution

	2% diltiazem		2% Lignocaine		Total	
	Male	Female	Male	Female	N	%
<40	12 (60%)	4 (40%)	9 (60%)	9 (60%)	34	56.67%
>40	8 (40%)	6 (60%)	6 (40%)	6 (40%)	26	43.33%
Total	20 (100%)	10 (100%)	15 (100%)	15 (100%)	60	100%

Age and gender wise distribution shows, out of the 20 male participant in the Diltiazem group 60% were in <40 year category and 40% in >40 year group.
In the 2% Lignocaine, 60% belong to <40 year and 40% belong to >40 year

Out of the 10 female in the Diltiazem group, 40% in <40 year and 60% >40 year.
In the 2% Lignocaine, 60% belong to <40 year and 40% belong to >40 year

Table 4: Pain

	2% diltiazem		2% Lignocaine		Total	
	N	%	N	%	N	%
Yes	22	73.3%	21	70%	43	71.7%
No	8	26.7%	9	30%	17	28.3%
Total	30	100%	30	100%	60	100%
Duration of Pain	6.62 ± 3.99		6 ± 3.46			
Chi square test = 0.08 , p=0.77 , Not statistically significant						

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Distribution based on pain on presentation shows in the Diltiazem group 73.3% had pain and in 2% Lignocaine 70% had pain.
The mean duration of pain in months in Diltiazem group was 6.62 ± 3.99 and in the 2% Lignocaine was 6 ± 3.46.

There was no statistically significant association observed between two groups with relation to pain as the p value calculated to be >0.05.

Table 5: Preoperative Pain score

	2% diltiazem		2% Lignocaine		Total	
	N	%	N	%	N	%
3	2	9.1%	2	9.5%	4	9.3%
4	8	36.4%	7	33.3%	15	34.9%
5	8	36.4%	8	38.1%	16	37.2%
6	2	9.1%	2	9.5%	4	9.3%
7	2	9.1%	1	4.8%	3	7%
8	0	0.0%	1	4.8%	1	2.3%
Total	22	100%	21	100%	43	100%
Mean ± SD	4.72 ±1.07		4.81 ±1.20		4.76 ± 1.13	
t test = 0.26 , p=0.79 , Not statistically significant						

The mean pre operative pain score in the Diltiazem group was 4.72 ±1.07 and in 2% Lignocaine was 4.81 ±1.20.

There was no statistically significant association observed between two groups with relation to pain score as the p value calculated to be >0.05.

Table 5: Bleeding per Rectum

	2% diltiazem		2% Lignocaine		Total	
	N	%	N	%	N	%
Yes	29	96.7%	26	86.7%	55	91.7%
No	1	3.3%	4	13.3%	5	8.3%
Total	30	100.0%	30	100.0%	60	100%
Duration in months	6.30 ± 3.32		5.56 ± 3.18			
Chi square test = 1.93 p=0.16 , Not statistically significant						

Distribution based on bleeding per Rectum on presentation, in the Diltiazem group it was 96.7% and in 2% Lignocaine 86.7% had bleeding per rectum.

The mean duration of bleeding per Rectum in months in Diltiazem group was 6.30 ± 3.32 and in the 2% Lignocaine was 5.56 ± 3.18

There was no statistically significant association observed between two groups with relation to bleeding per rectum as the p value calculated to be >0.05.

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Table 6: Constipation

	2% diltiazem		2% Lignocaine		Total	
	N	%	N	%	N	%
Yes	22	73.3%	20	66.7%	42	70%
No	8	26.7%	10	33.3%	18	30%
Total	30	100.0%	30	100.0%	60	100%
Duration	10.93 ±8.06		9.20 ±7.57			
Chi square test = 0.31, p=0.57 , Not statistically significant						

Distribution based on constipation on presentation, in the Diltiazem group it was 73.3% and in 2% Lignocaine 66.7%

The mean duration of constipation in months in Diltiazem group was 10.93 ±8.06 and in the 2% Lignocaine was 9.20 ±7.57

There was no statistically significant association observed between two groups with relation to constipation as the p value calculated to be >0.05.

Table 7: Pruritus

	2% diltiazem		2% Lignocaine		Total	
	N	%	N	%	N	%
Yes	2	6.7%	3	10.0%	5	8.3%
No	28	93.3%	27	90.0%	55	91.7%
Total	30	100.0%	30	100.0%	60	100%
Duration	2.50 ± 0.70		2 ± 1.0			
Chi square test = 0.21, p=0.64 , Not statistically significant						

Distribution based on pruritus on presentation, in the Diltiazem group it was 6.7% and in 2% Lignocaine 10%

The mean duration of pruritus in months in Diltiazem group was 2.50 ± 0.70 and in the 2% Lignocaine was 2 ± 1.0

There was no statistically significant association observed between two groups with relation to pruritus as the p value calculated to be >0.05.

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Table 8: Past History

	2% diltiazem		2% Lignocaine	
	N	%	N	%
TB	0	0%	0	0%
IBD	0	0%	0	0%
PPAS	0	0%	0	0%
Pregnancy	0	0%	0	0%
CVS Surgery	0	0%	0	0%

Table 9: Personal history

		2% diltiazem		2% Lignocaine		P value
		N	%	N	%	
Fibre Diet	High	0	0.0%	0	0.0%	-
	Low	30	100.0%	30	100.0%	
Fluid intake	< 1	8	26.7%	8	26.7%	0.98
	> 1	4	13.3%	4	13.3%	
	<1.5	7	23.3%	6	20.0%	
	>1.5	11	36.7%	12	40.0%	
Alcohol	Yes	15	50.0%	14	46.7%	0.79
	No	15	50.0%	16	53.3%	
Smoker	Yes	6	20.0%	5	16.7%	0.74
	No	24	80.0%	25	83.3%	
Bowel habits	Regular	8	26.7%	7	23.3%	0.76
	Irregular	22	73.3%	23	76.7%	

100% of both the groups were on low fibre diet.
Distribution based on fluid intake, in the Diltiazem group 63.3% <1.5 litre fluid intake and 36.7% had >1.5 litre fluid intake. And in the 2% Lignocaine, 60% had fluid intake <1.5 litre fluid intake and 40 % with >1.5 litre fluid intake.

50% of the Diltiazem group had alcohol intake and 46.7% of 2% Lignocaine had alcohol intake.
20% of the Diltiazem group were smokers and 16.7% of 2% Lignocaine were smokers
26.7% in the Diltiazem group and 23.3% in the 2% Lignocaine had regular bowel habits.

Table 10: Inspection

		2% diltiazem		2% Lignocaine		P value
		N	%	N	%	
Fissure site	Anterior	6	20.0%	3	10.0%	0.38
	Posterior	24	80.0%	25	83.3%	
	Anterior + Posterior	0	0.0%	2	6.7%	

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Number	1	30	100.0%	30	100.0%	-
Sentinel pile	Yes	27	90.0%	27	90.0%	1
	No	3	10.0%	3	10.0%	
Discharge	Yes	2	6.7%	3	10.0%	0.64
	No	28	93.3%	27	90.0%	
Fistulous opening	Yes	0	0.0%	0	0.0%	-
	No	30	100.0%	30	100.0%	

Based on fissure site, Anterior in 20% in Diltiazem group and 10% in 2% Lignocaine. Posterior in 80% in Diltiazem group and 83.3% in 2% Lignocaine. Anterior + Posterior in 6.7% of 2% Lignocaine.
100% of the Lignocaine and Diltiazem group had 1 fissure.
90% of both the groups had sentinel pile.
6.7% and 10% had discharge present.
Fistulous opening was not present in the study participants in both the groups.

Table 11: Palpation

		2% diltiazem		2% Lignocaine		P value
		N	%	N	%	
Tenderness	Yes	9	30.0%	11	36.7%	0.58
	No	21	70.0%	19	63.3%	
Anal tone	Spasm	3	10.0%	4	13.3%	0.69
	Normal	27	90.0%	26	86.7%	
Induration	Yes	0	0.0%	0	0.0%	-
	No	30	100.0%	30	100.0%	
Discharge	Yes	2	6.7%	3	10.0%	0.64
	No	28	93.3%	27	90.0%	

30% of the Diltiazem and 36.7% of Lignocaine group had tenderness on palpation.
10% of the Diltiazem and 13.3% of 2% Lignocaine had abnormal anal tone.
6.7% of the Diltiazem and 10% of 2% Lignocaine had discharge

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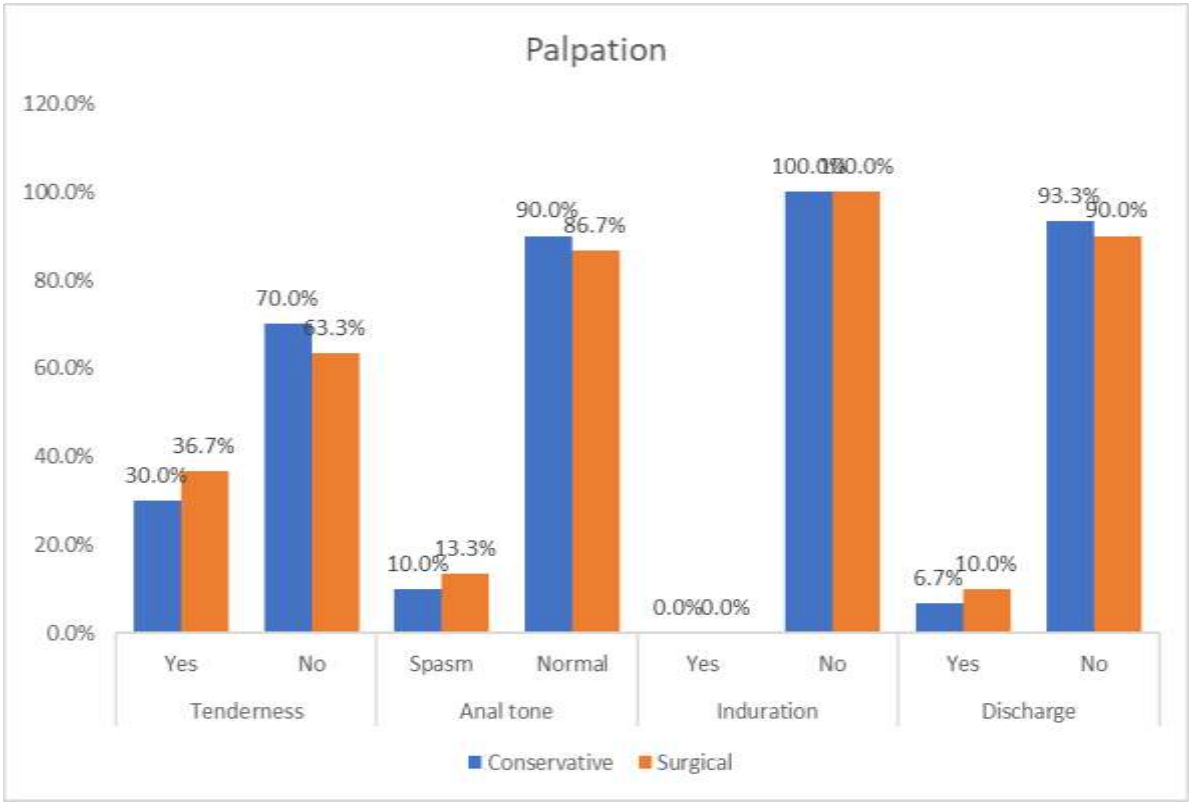

Table 12: Proctoscopy

		2% diltiazem		2% Lignocaine		P value
		N	%	N	%	
Anal mucosa	Normal	30	100.0%	30	100.0%	-
	Abnormal	0	0.0%	0	0.0%	
Haemorrhoids	Yes	2	6.7%	4	13.3%	0.39
	No	28	93.3%	26	86.7%	
Internal opening	Yes	0	0.0%	0	0.0%	-
	No	30	100.0%	30	100.0%	

6.7% of the Diltiazem and 13.3% of 2% Lignocaine had Hemorroids.

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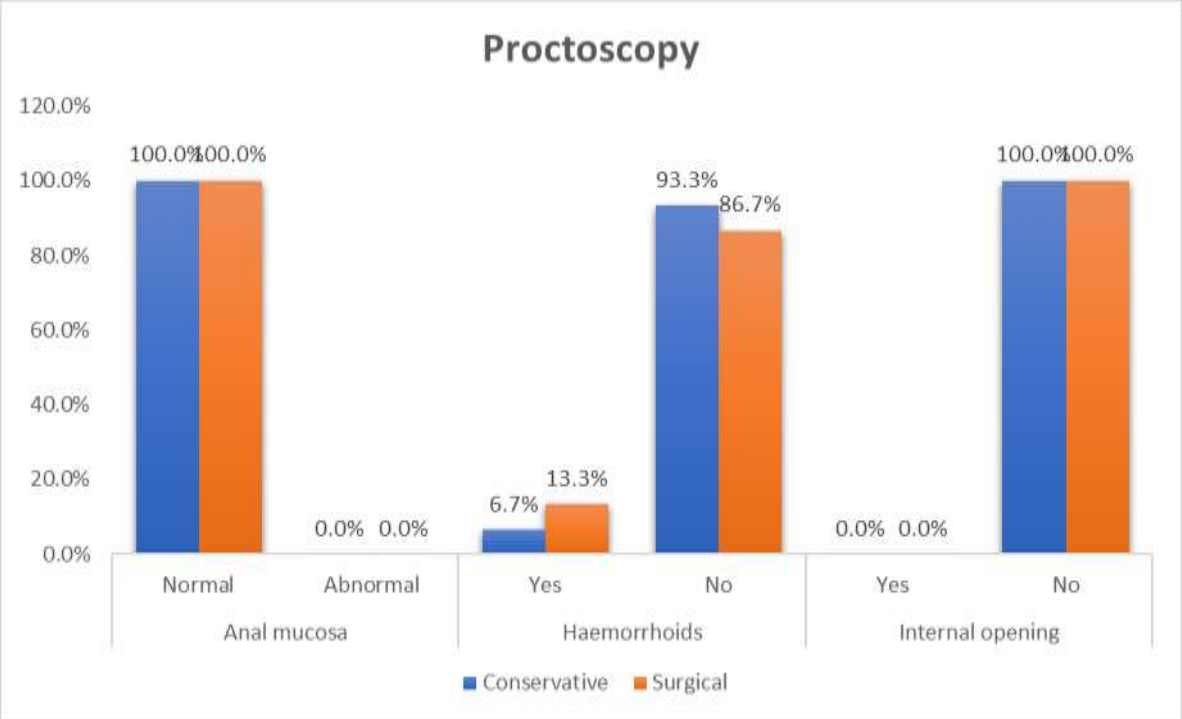

Table 13: Post operative follow up : 2 weeks

		2% diltiazem		2% Lignocaine		P value
		N	%	N	%	
Relief from pain	Yes	18	85.7%	16	72.7%	0.12
	No	3	14.3%	6	27.3%	
Bleeding per Rectum	Yes	24	82.7%	20	76.9%	0.24
	No	5	20.0%	6	23.1%	
Anal incontinence	Yes	0	0.0%	0	0.0%	-
	No	30	100.0%	30	100.0%	

In the present study, 85.7% in Diltiazem group and 72.7% in 2% Lignocaine had relief from pain after 2 weeks of follow up.

82.7% in the Diltiazem group and 76.9% in 2% Lignocaine had bleeding per rectum

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Table 14: Post operative follow up : 4 weeks

		2% diltiazem		2% Lignocaine		P value
		N	%	N	%	
Relief from pain	Yes	20	95.2%	18	81.8%	0.13
	No	1	4.8%	4	18.2%	
Bleeding per Rectum	Yes	26	89.6%	22	84.6%	0.72
	No	3	10.4%	4	15.4%	
Anal incontinence	Yes	0	0.0%	0	0.0%	-
	No	30	100.0%	30	100.0%	

In the present study, 95.2% in Diltiazem group and 81.8% in 2% Lignocaine had relief from pain after 4 weeks of follow up.

89.6% in the Diltiazem group and 84.6% in 2% Lignocaine had bleeding per rectum

Table 15: Post operative follow up : 3 months

		2% diltiazem		2% Lignocaine		P value
		N	%	N	%	
Relief from pain	Yes	21	100.0%	20	90.9%	1
	No	0	0.0%	2	9.1%	
Bleeding per Rectum	Yes	25	96.1%	27	93.1%	0.55
	No	2	7.7%	2	6.9%	
Anal incontinence	Yes	0	0.0%	0	0.0%	-
	No	30	100.0%	30	100.0%	

In the present study, 100% in Diltiazem group and 90.9% in 2% Lignocaine had relief from pain after 4 weeks of follow up.

93.1% in the Diltiazem group and 96.1% in 2% Lignocaine had bleeding per rectum

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Table 16: Post operative follow up

		2% diltiazem		2% Lignocaine		P value
		N	%	N	%	
Relief from pain	2 weeks	18	85.7%	16	72.7%	0.04*
	4 weeks	20	95.2%	18	81.8%	
	3 months	21	100.0%	20	90.9%	
Bleeding per Rectum	2 weeks	24	82.7%	20	76.9%	0.04*
	4 weeks	26	89.6%	22	84.6%	
	3 months	27	93.1%	25	96.1%	

Significant difference observed with relation to relief from pain and bleeding per rectum in both the groups as the p value calculated to be <0.05.

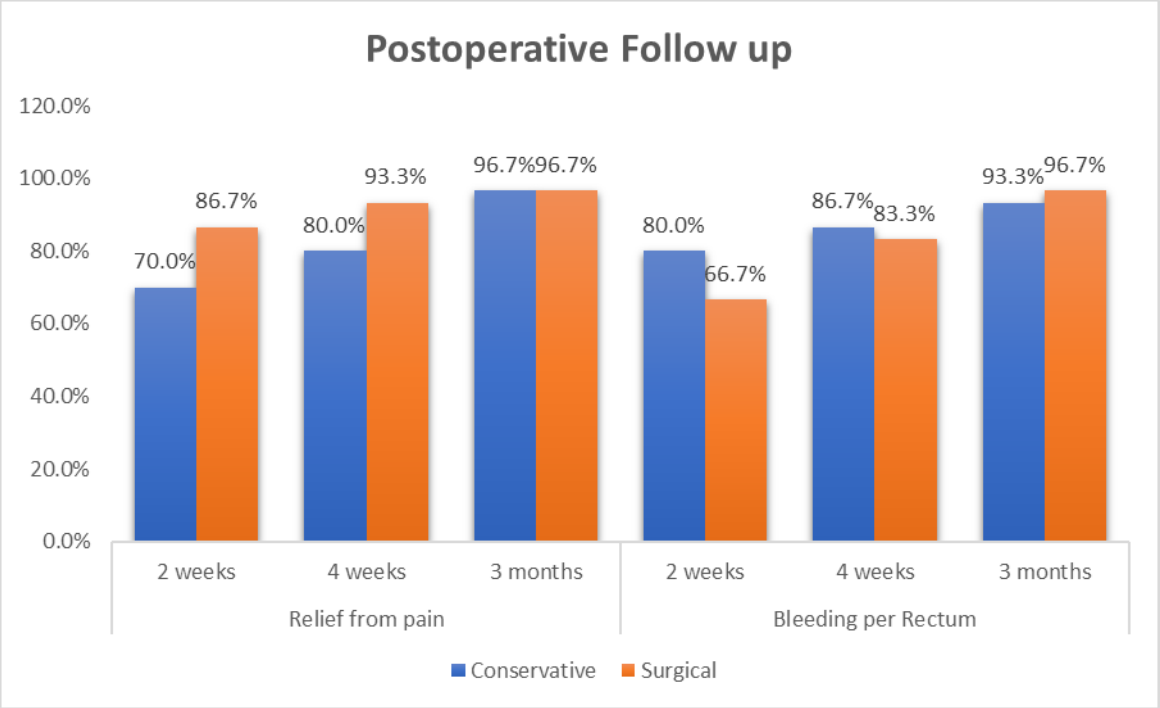

Table 17: Healing of Fissure

	2% diltiazem		2% Lignocaine	
	N	%	N	%
2nd week	0	0%	0	0%

4th week	19	63.3%	12	40%
3 months	30	100%	27	90%
Total	30	100.0%	30	100.0%

Table 17: Recurrence

	2% diltiazem		2% Lignocaine		Total	
	N	%	N	%	N	%
Yes	0	0%	3	10%	3	5%
No	30	100%	27	90%	57	95%
Total	30	100.0%	30	100.0%	60	100%
Chi square test = 3.10, p=0.07 , Not statistically significant						

IV. DISCUSSION

Anal fissures are considered one of the commonest causes of severe anal pain. An anal fissure is a longitudinal tear or ulcer in the distal anal canal. It is usually located in the posterior or anterior midline and extends from the level of dentate line to the anal verge. Acute fissure is one which presents within 3-6 weeks of symptom onset. It has the appearance of a clean longitudinal tear in the anoderm with little surrounding inflammation. Acute fissure usually heals spontaneously within 6 weeks. A chronic fissure, with more than 6 weeks of symptoms, is usually deeper and generally has exposed internal sphincter fibers in its base[56]

It is frequently associated with a hypertrophic anal papilla at its upper aspect and sentinel pile at its distal aspect. Based on etiology it is classified as primary (idiopathic) or secondary. Secondary fissures are those that occur due to some other pathology such as Crohn's disease, anal tuberculosis, AIDS. Patients usually present with pain during defecation and passage of bright red blood per anus[57]

The precise etiology of anal fissure is unknown. Fissure is most commonly attributed to trauma from the passage of a large hard stool, but it is also seen after acute episodes of diarrhea. Painful fissures are generally associated with involuntary spasm of the internal sphincter with high resting pressure in the anal canal. So it seems that chronic over activity of the internal sphincter may be the cause. Reduction of anal sphincter spasm results in improved blood supply and healing of fissure. Surgical techniques like manual anal dilatation or lateral internal sphincterotomy, effectively heal most fissures within a few weeks but may result in permanently impaired anal continence. This has led to the research for alternative non-surgical treatment, and various pharmacological agents such as nitrates (glyceryl trinitrate, isosobide dinitrate), calcium channel blockers (nifedepine, diltiazem) have been shown to lower resting anal pressure and heal fissures without threatening anal continence.[58] The present study compares the effectiveness and side effects topical application of 2% diltiazem versus 2% lignocaine in the treatment of chronic fissure in ano.

V. CONCLUSION

Our study clearly demonstrates that adding topical Diltiazem in the treatment of anal fissure is far superior to treatment with only topical Lignocaine. It is significantly better in control of pain, has better healing rates and is more effective in control of bleeding. Although both Lignocaine and Diltiazem are almost identical in these parameters, lignocaine is better tolerated with lower incidence of adverse reactions.Thus, we

recommend the topical use of CCBs as first line therapy in the management of anal fissures.

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