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Original Research Article

Comparison of topical agents minoxidil and diltiazem in medical management of anal fissures: a hospital based study

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ABSTRACT

Background: Anal fissures are associated with spasm of the internal anal sphincter and pain. In present study we compared the efficacy of local application of 0.5% minoxidil and 2% diltiazem in symptomatic relief and healing of anal fissures.
Methods: In this prospective, randomized, double blind study, a total of 100 patients with anal fissure were recruited, (50 patients in each group). Patients in group A received local applications of ointments containing 0.5% minoxidil, while patients in group B received topical 2% Diltiazem. Healing of anal fissure and symptomatic relief were observed and analyzed.
Results: Rates of complete healing of fissure were similar in the two groups (minoxidil 27/50, diltiazem 29/50). Mean (SD) time taken for complete healing was significantly shorter with minoxidil (3.1 weeks as compared to diltiazem (4 weeks). Rates of pain relief were similar in the two groups. Stoppage of bleeding occurred more often with use of minoxidil than with diltiazem. No patient had systemic or local side effects.
Conclusions: Treatment with minoxidil helps in faster healing of anal fissures and provides similar symptomatic relief as that of diltiazem.

Keywords: Diltiazem, Internal anal sphincter (IAS), Minoxidil

INTRODUCTION

Anal fissure is a tear in the anal mucosa extending from the anal verge towards the dentate line. It was first described by Recamier in the year 1829. It is common in people of all ages and especially in teenagers and young adults. Studies suggest that as many as one in five people develop anal fissure during their lifetime.

Anal fissure occurs predominantly in the midline and most commonly posterior (90%) with 10% anterior. After childbirth, women tend to have an anterior fissure, and less than 1% of patients have fissure both in the anterior and posterior positions.[1] The basic underlying cause for anal fissure is increased tone of the internal anal sphincter (IAS) and pain; this vicious cycle of pain and spasm leads to reduced mucosal blood flow and hence to poor healing of the fissure.[2]

Ulcers can be inspected by gently parting the posterior anus. Digital and proctoscopic examination is avoided as it triggers severe pain and spasm of the underlying muscle. Histologically, one can see acute and chronic infection and granulation tissue. There is presence of sentinel tag is a fibroepithelial polyp covered by squamous mucosa.[3]

Surgery to reduce the increased anal tone has been the standard treatment for anal fissure. However, surgical procedures are associated with significant morbidity such

as fecal incontinence.[4] Several drugs, such as glyceryl trinitrate (GTN), botulinum toxin, isosorbide dinitrate, L-arginine, and calcium-channel blockers, have been used to reduce the IAS tone till the fissure heals.[5-10]

Since minoxidil, a potassium-channel opener used in the treatment of hypertension and male pattern baldness, induces smooth muscle relaxation and vasodilatation.[11-13] we aspired to check its efficacy vis a vis a topical calcium channel blocker (diltiazem) in treatment of anal fissures.

METHODS

Consecutive patients of either gender aged 15-60 years presenting to our outpatient department between August 2015 and September 2017 with features of acute anal fissure were included in the study. Chronic anal fissures were excluded from the study, Chronic fissure was defined as one with symptoms lasting more than one month, induration of the fissure, visible fibers of sphincter muscle at base of fissure, and presence of a sentinel pile.[5,10] Patients with cardiovascular diseases, pregnant and lactating mothers, and patients with anal disease that warranted surgery, such as abscess or fistula, were also excluded.

This was a prospective, randomized, double blind controlled study. The ethics committee of our hospital approved the protocol and all patients provided written informed consent. Eligible patients were assigned to one of the two treatment groups according to a computer-generated randomization list. The drugs were prepared as ointments in a soft white paraffin base. The two treatment groups received one of the two ointments: (a) 0.5% minoxidil (b) 2%diltiazem. Patients were advised to apply about 0.5 g of the ointment circumferentially inside the anal orifice every 8 hours for 6 weeks; no laxatives or stool softeners were prescribed during the trial period. The patients were asked to visit the hospital every week for a period of 6 weeks. Anal pain was assessed before starting treatment and at weekly follow-up visits using a linear visual analog pain score (range 0-10).

Bleeding per rectum was assessed subjectively at baseline and at the end of treatment. Pulse rate, blood pressure and any side effects associated with treatment were recorded at each visit. Complications that were specifically looked for were postural hypotension, perianal dermatitis, hypertrichosis, and allergy to the drug. The primary endpoint was complete healing of anal fissures, defined as presence of scar at 6 weeks of treatment. Partial healing was defined as persistence of fissure but with improvement in symptoms (pain relief and/or control of bleeding). At the end of the trial, patients who had not responded were advised surgical treatment.

Statistical analysis

SPSS Software 10.0 were used for statistical analysis. P value <0.05 was considered significant.

RESULTS

Of the total of 100 patients, patients were randomly assigned to one of the two groups,50 patients belonging to group A received 0.5% minoxidil and 50 patients belonging to group B received 2% diltiazem. The mean age of the patients in group A was 36.2 years and that in group B was 38.1 years, the difference was statistically insignificant. The gender ratio in group A and B was 36/14 and 32/18 male /female respectively, the difference was statistically insignificant (Table 1).

Table 1: Patient parameters.

Name of the group	No. of patients	Mean age in years	Male/female
Group A	50	36.2	36/14
Group B	50	38.1	32/18

The dominant symptom in both the groups was pain on defecation, with 20/50 (40%) patients in group A and 18/50 (36%) patients in group B complaining of painful defecation as the main symptom. The other major symptoms were bleeding per rectum, anal discomfort, and constipation respectively (Table 2).

Table 2: Dominant symptom.

Name of the group	Pain	Bleeding	Discomfort	Constipation
Group A	20	22	6	2
Group B	18	17	9	6

All patients were compliant with the study and followed with great deal of interest. Rates of complete and partial healing of anal fissure were comparable in the two groups (p >0.05).

Table 3: Results.

Parameters	0.5% Minoxidil (Group A)	2% Diltiazem (Group B)
Healing		
Complete	27 (54%)	29 (58%)
Partial	15 (30%)	16 (32%)
None	8 (16%)	5 (10%)
Time to complete healing	3.1 weeks	4 weeks
Pain relief	17/20 (85%)	15/18 (83.3%)
Stoppage of bleeding	19/22 (86.3%)	11/17 (64.7%)

The time taken to achieve complete healing was shorter in the group A (3.1 weeks) than in group B (4 weeks). Rates of pain relief were similar in the two groups; however, the proportion with stoppage of bleeding was higher with minoxidil therapy than with diltiazem (Table 3).

DISCUSSION

Minoxidil, is a pyrimidine derivative, it is a vasodilator and smooth muscle relaxant that also possesses trichogenic properties.[11-13] We know this drug, can promote healing of anal fissure by relieving internal anal sphincter spasm and pain. This drug has been previously used in the treatment of anal fissures. In our study, minoxidil led to complete healing of fissures in 54% of patients and partial healing in 30%. This complete healing rate was lower than that reported previously with 0.2% glyceryl trinitrate (GTN; 59%-70%).[14,15]

However, there were no disabling side effects that are observed with GTN and result insignificant treatment failure. Fissure healing was complete in 58% of patients receiving topical diltiazem. The mean time taken for complete healing of fissures with 0.5% minoxidil was only 3.1 weeks, which was significantly shorter than with topical diltiazem. In comparison, time taken has been reported to be 2-3 weeks with lateral sphincterotomy, 4-7 weeks with posterior sphincterotomy, and 2-3 months with topical GTN applications.[14,15]

In a prospective, randomized, double-blind study, conducted by Rajakannu M et al, 90 patients with AF were recruited. Patients received local applications of ointments containing 5% lignocaine (N=28), 0.5% minoxidil (N=36), or both (N=26) (78). Healing of AF at 6wk was considered as the primary end point. The healing rate was similar in the three groups. However, the mean time taken for complete healing with combination treatment (1.9 wk) was significantly shorter than that with minoxidil alone (3.1 wk, P=0.001) or with lignocaine alone (3.3 wk, P=0.002). Thus, a combination of minoxidil and lignocaine helped in faster healing of AF and provided better symptomatic relief than either drug alone.[16]

In a study carried out by Knight *et al*., 71 consecutive patients with CAF were treated with DTZ (2%) ointment for 9 wk. About 88% of patients healed with DTZ ointment. Four patients experienced perianal dermatitis and one patient suffered from headache. After 32 wk completion of the treatment, 27 of 41 patients available remained symptom-free. Six of the seven patients with recurrent fissure were treated successfully by repeating DTZ treatment.[17]

Our results are in agreement with that of previous similar studies. The minoxidil group had slightly higher rate of pain relief than did diltiazem, but the difference was statistically insignificant. Besides, bleeding stopped in significantly greater proportion of patients treated with 0.5% minoxidil (86.3%) as compared with 2% diltiazem (64.7%). Decrease in bleeding has also been reported after 2 weeks of treatment with oral or topical diltiazem in other previous studies.[9] The small sample size is the main limiting factor of our study.

CONCLUSION

Study data show that therapy with 0.5% minoxidil is a very effective type of medical therapy in the management of anal fissures with significantly quick results and minimum side effects.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Kodner IJ, Fry RD, Fleshman JW. Colon rectum and anus. In: Schwartz's Principles of Surgery. 7th edition. USA: McGraw Hill; 1999:1265.
2. Gibbons CP, Read NW. Anal hypertonia in fissures: cause or effect? Br J Surg. 1986;73:443-5.
3. Klosterhalfen B, Vogel P, Rixen H, Mittermayer C. Topography of the inferior rectal artery: a possible cause of chronic, primary anal fissure. Dis Colon Rectum. 1989;32:43-52.
4. Lewis TH, Corman ML, Prager ED, Robertson WG. Long term results of open and closed sphincterotomy for anal fissure. Dis Colon Rectum. 1988;31:368-71.
5. Lund JN, Armitage NC, Scholefield JH. Use of glyceryl trinitrate ointment in the treatment of anal fissure. Br J Surg. 1996;83:776-7.
6. Schouten WR, Briel JW, Boerma MO, Auwerda JJ, Wilms EB, Graatsma BH. Pathophysiological aspects and clinical outcome of intra-anal application of isosorbide-dinitrate in patients with chronic anal fissure. Gut. 1996;39:465-9.
7. Jost WH, Schimrigk K. Therapy of anal fissure using botulin toxin. Dis Colon Rectum 1994;37:1321-4.
8. Antropoli C, Perrotti P, Rubino M, Martino A, De Stefano G, Migliore G, et al. Nifedipine for local use in conservative treatment of anal fissures: preliminary results of the multicentre study. Dis Colon Rectum. 1999;42:1011-5.
9. Jonas M, Neal KR, Abercrombie JF, Scholefield JH. A randomized trial of oral vs. topical diltiazem for chronic anal fissure. Dis Colon Rectum. 2001;44:1074-8.
10. Maan MS, Mishra R, Thomas S, Hadke NS. Randomized, double-blind trial comparing topical nitro-glycerine with xylocaine and Proctosedyl in idiopathic chronic anal fissure. Indian J Gastroenterol. 2004;23:91-3.
11. Meisheri KD, Cipkus LA, Taylor CJ. Mechanism of action of minoxidil sulfate-induced vasodilatation: a role for increased K+ permeability. J Pharmacol Exp Ther. 1988;245:751-60.
12. Wester RC, Maibach HI, Guy RH, Novak F. Minoxidil stimulates cutaneous blood flow in human balding scalps: pharmacodynamics measured by laser Doppler velocimetry and photo pulse

plethysmography. J Invest Dermatol. 1984;82:515-7.
13. Eller MG, Szpunar GJ, Della-Coletta AA. Absorption of minoxidil after topical application. Clin Pharmacol Therap. 1989;45:396-402.
14. Notaras MJ. The treatment of anal fissure by lateral subcutaneous internal sphincterotomy for anal fissure. Br J Surg. 1971;58:96-100.
15. Kennedy ML, Sowter S, Nguyen H, Lubowski DZ. Glyceryl trinitrate ointment for the treatment of chronic anal fissure. Dis Colon Rectum. 1999;42:1000-6.
16. Rajakannu M, Robinson Smile S, Sistla SC, Raveendran R. Treatment of anal fissures using a combination of minoxidil and Lignocaine. Indian J Gastroenterol. 2005;24:158-60.
17. Knight JS, Birks M, Farouk R. Topical diltiazem ointment in the treatment of chronic anal fissure. Br J Surg. 2001;88:553-6.

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