Aim: Anal fissures are associated with hypertonia of the internal anal sphincter and pain. We evaluated the efficacy of local application of a combination of minoxidil and lignocaine in healing anal fissures.

Methods: In this prospective, randomized, double-blind study, 90 patients with anal fissure were recruited. Patients received local applications of ointments containing 5% lignocaine (n=28), 0.5% minoxidil (n=36), or both (n=26). Healing of anal fissure at 6 weeks was used as the primary end-point. Results: Rates of complete healing of fissure were similar in the three groups (lignocaine alone 8/27, minoxidil alone 10/34, combination 7/22; p=ns). Mean (SD) time taken for complete healing with combination treatment [1.9 (0.6) weeks] was significantly shorter than that with minoxidil alone (3.1 [1.7] weeks; p=0.001) or with lignocaine alone (3.3 [0.8] weeks; p=0.002). Rates of pain relief were similar in the three groups. Stoppage of bleeding occurred more often with combination treatment than with lignocaine alone. No patient had systemic or local side effects. Conclusion: Combination treatment with minoxidil and lignocaine helps in faster healing of anal fissures and provides better symptomatic relief than either drug alone. [Indian J Gastroenterol 2005; 24:158-160]
Treatment of anal fissure

Indian Journal of Gastroenterology 2005 Vol 24 July - August   159

Rajakannu, Robinson, Sistla, Raveendran

pain). Bleeding per rectum was assessed subjectively at baseline and at the end of treatment. Anal manometry was performed at baseline and every two weeks thereafter till the end of treatment using the technique described by Saraiva et al. This simple bedside method is based on the flow of air in an open circuit established by connecting (by a T junction) a rubber probe with a side opening at its tip which is covered by a finger stall to a syringe for pumping air and an arterial pressure gauge. The rubber probe mounted with the fingerstall is placed into the anal canal without anesthetic lubrication and air is pumped slowly by closing the syringe piston. As the air is pumped, it is conveyed through the tip opening and the protective stall is inflated until the internal anal sphincter pressure is overcome. At this time the excess air escapes from the fingerstall, producing a peculiar sound. By this method resting anal pressure is measured when the patient is relaxed and squeeze pressure when the patient is straining. This method was standardized and validated before starting the trial by measuring the anal pressure in normal subjects and fissure patients at our institute.

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

Statistical Package for Social Sciences 10.0 (SPSS/PC, SPS, Chicago, USA) and Epi-Info Software 6.0 were used for statistical analysis. Chi-squared test was used to compare proportions between groups. Unpaired t test was used to compare the decrease in mean resting anal pressure (MRAP) between the three groups before and after treatment, and paired t test was used to assess reduction in MRAP after treatment. One-way ANOVA with a post-hoc test (least significant difference) was used to compare the time taken for complete healing in the three groups. p value <0.05 was considered significant.

Results

Of the 90 patients recruited, seven (4 of 26 in the combination group, 1 of 28 in lignocaine group, and 2 of 36 in minoxidil group) did not follow up. Data were therefore analyzed for only 83 patients.

Rates of complete and partial healing of anal fissures were comparable in the three groups (Table). The time taken to achieve complete healing was shorter in the combination group than in the other two groups (Table). Rates of pain relief were similar in the three groups; however, the proportion with stoppage of bleeding was higher with combination therapy than with lignocaine alone. Pre-treatment mean resting anal pressures were comparable in the three groups. These decreased significantly in all the three groups after treatment (p<0.0001 for each); however, the post-treatment pressures were similar in the three groups. No patient reported any local or systemic adverse event.

Discussion

Minoxidil, a pyrimidine derivative, is a vasodilator and smooth muscle relaxant that also possesses trichogenic properties. We proposed that this drug, when used in combination with lignocaine, a local anesthetic, could promote healing of anal fissure by relieving internal anal sphincter spasm and pain. This drug had not been previously used in the treatment of anal fissures.

In our study, lignocaine and minoxidil combination led to complete healing of fissures in 32% of patients and partial healing in 50%. This complete healing rate was lower than that reported previously with 0.2% glyceryl trinitrate (GTN; 59%-70%); however, there were no disabling side effects that are observed with GTN and result in significant treatment failure. Fissure healing was complete in 38% of patients receiving oral diltiazem.
and 65% of those receiving topical diltiazem treatment for eight weeks.\(^1^3\)

The mean time taken for complete healing of fissures was only 1.9 weeks, which was significantly shorter with the minoxidil-lignocaine combination than with individual drugs. 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.\(^3^,^4^,^1^7^-^2^0\) In a study by Singh et al, only 3 of 16 patients had complete healing at 4 weeks with GTN.\(^1^1\)

Faster complete healing of fissures with minoxidil-lignocaine combination in our study was probably related to synergistic action of the two drugs, i.e., minoxidil relieving the internal anal sphincter spasm and improving blood supply, and lignocaine inducing pain relief.

Jensen showed that 2% lignocaine caused symptomatic relief in 70% of patients over three weeks.\(^2^1\) Antropoli et al used topical nifedipine and reported that pain disappeared in 60% of patients and decreased in 30% of patients after 21 days of treatment.\(^8\) In the present study, the minoxidil-lignocaine combination led to better pain relief than did lignocaine or minoxidil monotherapy. Besides, bleeding stopped in all patients treated with this combination. Decrease in bleeding has also been reported after 2 weeks of treatment with oral or topical diltiazem.\(^1^0\)

The small sample size is the main limiting factor of our study. Another limitation is the use of per-protocol analysis instead of intention-to-treat analysis.

In conclusion, our data show that combination therapy with minoxidil and lignocaine improves the rate of healing of anal fissures.

References
19. Carapeti EA, Kamm MA, Mc Donald PS, Chadwick SJ, Melville D, Phillips RK. Randomised controlled trial shows that glyceryl trinitrate heals anal fissures, higher doses are not more effective, and there is a high recurrence rate. Gut 1999;44:727-30.