Glyceryl Trinitrate vs. Sphincterotomy for Treatment of Chronic Fissure-In-Ano

A Randomized, Controlled Trial

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PURPOSE: This study was undertaken to compare local application of a glyceryl trinitrate ointment with lateral internal sphincterotomy for the treatment of chronic fissure-in-ano. PATIENTS AND METHODS: A sample of 24 consecutive patients with chronic anal fissure was randomly allocated to treatment with sphincterotomy or local glyceryl trinitrate. Patients were followed-up for a median of 22 months. RESULTS: All 12 patients healed following sphincterotomy; 10 of 12 healed with local glyceryl trinitrate (P = 0.239). There were no recurrences or side-effects in either group. CONCLUSIONS: Local application of glyceryl trinitrate can avoid surgery in more than 80 percent of patients with chronic anal fissure. [Key words: Fissure-in-ano, chronic, anal fissure; Glyceryl trinitrate; Sphincterotomy, anal]


The conservative treatment of chronic fissure-in-ano includes local anesthesia, graduated dilators, and bulking agents. For effective therapy, however, it is necessary to break the vicious cycle of pain, sphincter spasm, and ischemia, usually by internal sphincterotomy.

Because of the occasional complications (minor degrees of incontinence for flatus), attempts have been made at "chemical sphincterotomy." Local injection (into the external anal sphincter) of botulinum toxin is the best known of these but has not achieved wide popularity. Most surgeons remain faithful to the simple and very effective lateral internal sphincterotomy.

Demonstration that nitric oxide is the inhibitory neurotransmitter of the internal anal sphincter opened further possibilities, which have been explored in uncontrolled studies. Glyceryl trinitrate (GTN) is a well-known nitric oxide donor, although perhaps more familiar to cardiologists and anesthesiologists than proctologists. This trial compared local application of a GTN ointment with formal sphincterotomy in the treatment of chronic fissure-in-ano.

SUBJECTS AND METHODS

The sample comprised 24 consecutive patients presenting with chronic fissure-in-ano, who had had no previous treatment for the fissure. A table was constructed whereby the odd-numbered patients (first, third, fifth, . . .) were randomly allocated (by random number tables) to either local GTN treatment or sphincterotomy. The even-numbered patients (second, fourth, sixth, . . .) received the opposite treatment to their immediate predecessor. This provided two samples of identical size.

The fissures were all "chronic" in that the duration of symptoms varied from a few weeks to several months. However, the essential characteristic was that sphincter fibers were invariably visible in the base of the fissure. Coincidentally, there were 12 men and 12 women, one-half of whom received each treatment. Mean age of those treated surgically was 40.1 (range, 22-55) years and of the GTN group 41.3 (range, 23-69) years. All fissures were posterior; none was associated with Crohn's disease, tuberculosis, or acquired immunodeficiency syndrome, and none had an associated abscess or fistula.

The sphincterotomy was performed in the standard fashion (subcutaneous lateral partial internal sphincterotomy). Patients were reviewed at one week and one month. There was a median long-term follow-up of 22 (range, 8-34) months.

A transdermal form of glyceryl trinitrate is not available in this country; we used Angised® (Wellcome, Midrand, South Africa) tablets, which contain 0.5 mg of GTN. One tablet was crushed in 10 ml of glycerine lubricating jelly (K-Y®; Johnson & Johnson, Midrand,
South Africa) and applied three times per day to the anal verge and up the anal canal. The solution was discarded after the evening dose and made up fresh each morning. Any patient not showing dramatic improvement at the first visit was seen one week later. If failure to improve persisted, surgery was performed two weeks after entering the trial.

The study had a power of 0.62 to detect a difference of 25 percent at a 5 percent level of significance. The protocol was approved by the Pharmacy and Therapeutics Committee of the hospital and the Human Ethics Committee of the University of the Witwatersrand.

**RESULTS**

All patients treated by sphincterotomy had complete healing by four weeks; there have been no recurrences during the period of follow-up (8–34 months) and no disturbances of continence. Pain relief was prompt, and all patients were discharged on the following day.

Of the group of patients treated with local glyceryl trinitrate, ten patients had prompt symptomatic relief, and all of these patients experienced healing by four weeks. The remaining two patients showed no improvement after two weeks, underwent sphincterotomy, and experienced rapid healing. All fissures-in-ano have remained healed. Pain relief was immediate in the “successes,” and there were no complications or disturbances with continence. An interesting observation is that those patients in whom the method failed indicated promptly that there was a lack of symptomatic relief. Although subjects in this study were given a two-week trial of GTN, it may well be possible to make a decision after one week or less and proceed to surgery as soon as possible. The success rate in the GTN-treated group was 0.83 (i.e., 10/12); the 95 percent confidence intervals of this result are 0.62–1.

Data were analyzed by Fisher’s one-tailed exact test (assuming that sphincterotomy would be the more effective treatment). There was no statistically significant difference in outcome between the two modalities ($P = 0.2391$), implying that the two forms of therapy are comparable. More than 80 percent of patients with a chronic fissure may be spared the necessity of undergoing a sphincterotomy by receiving a local application of glyceryl trinitrate ointment. If the test were two-tailed (both treatments regarded as equally effective), the $P$ value was 0.4783.

**DISCUSSION**

As early as 1951, Eisenhammer,8 who had also shown that Miles’ “pectenotomy” was an internal sphincterotomy, proposed a lateral sphincterotomy for fissure. Since the description of a subcutaneous approach by Notaras in 1969,7 there has been little change in the technique for the last 30 years. The main disadvantage of sphincterotomy as currently practiced is the definite, although small, incidence of incontinence for flatus.

Because the aim of surgery is to relieve sphincter spasm, alternative chemical means of spasmolysis have been sought. Local injection of botulinum toxin is one such method. This agent paralyzes the external sphincter by inhibiting acetylcholine release, an effect that lasts for some weeks until reinnervation occurs by sprouting of the nerve ends. One recent study found healing in 10 of 12 cases so treated.9

Local application of a nitric oxide donor is even more attractive. The drug is cheap and readily available; the effects are quickly reversible; patient response is rapidly apparent; the treatment avoids surgery in the majority of instances; failure does not prejudice the patient in any way; and side effects are insignificant.

We have not performed any pharmacokinetic studies on our concoction (Angised® in K-Y®) but have advised patients to make up the ointment daily. None has complained that the evening application seemed less effective than the first one of the day. Relief is dramatic, occurring soon after an application.

**CONCLUSION**

Local application of glyceryl trinitrate ointment will heal more than 80 percent of chronic anal fissures and can radically reduce the number of cases requiring sphincterotomy.

**REFERENCES**

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