Glyceryl trinitrate ointment increased healing and decreased pain in patients with chronic anal fissure


Objective
To evaluate the effectiveness of glyceryl trinitrate (GTN) ointment in the treatment of chronic anal fissure.

Design
Randomised, double-blind, placebo-controlled trial with 4-week follow-up after completion of treatment.

Setting
Surgical outpatient clinics at 2 hospitals in the United Kingdom.

Patients
80 consecutive patients (median age 35 yr, 55% women) who had symptoms of anal fissure for > 6 weeks with fibrosis at the base of the fissure. 95% completed the trial.

Intervention
39 patients were allocated to treatment with topical 0.2% GTN ointment to be applied to the lower anal canal twice daily, and 41 were allocated to identical placebo.

Main outcome measures
Healing of the fissure, level of pain on defaecation, maximum anal resting pressure (MARP), and anodermal blood flow.

Main results
Analysis was by intention to treat. After 8 weeks, anal fissures healed in 26 of 38 patients (68%) treated with GTN compared with 3 of 39 patients (7.7%) treated with placebo (P < 0.001) (Table). The linear analogue pain score was reduced at week 2 in the GTN group and continued to decrease throughout the study period. This persistent decrease was not seen in the placebo group. MARP measured just after first application, decreased from 115.9 cm H\(_2\)O to 75.9 cm H\(_2\)O in the GTN ointment group (P < 0.001) but stayed the same in the placebo group. Anodermal blood flow measured for 40 minutes after the first application increased in the patients treated with GTN ointment (P < 0.05) but stayed almost the same in the patients receiving placebo.

Conclusion
Glyceryl trinitrate ointment applied to the lower anal canal was effective in promoting healing and decreasing pain on defaecation in patients with chronic anal fissure.

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Glyceryl trinitrate (GTN) ointment vs placebo

<table>
<thead>
<tr>
<th>Outcome at 8 weeks</th>
<th>Glyceryl trinitrate (GTN)</th>
<th>Placebo</th>
<th>RBI (95% CI)</th>
<th>ABI (CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healing of anal fissures</td>
<td>68%</td>
<td>7.7%</td>
<td>789%</td>
<td>60.3%</td>
<td>2 (227 to 2526)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in Glossary; RBI, ABI, NNT, and CI calculated from data in article.

Commentary
Acute anal fissures are usually successfully treated with some combination of bulk ing agents, sitz baths, topical anaesthetics, topical corticosteroids, and emollient suppositories. Chronic anal fissures are associated with elevated resting anal pressure, although it is unknown whether this is a cause or effect. Persistent chronic anal fissures are usually treated with internal sphincterotomy, which has been shown to permanently reduce anal pressure and is extremely effective. However, some degree of incontinence occurs in some patients.

Glyceryl trinitrate, also known as nitroglycerin, is widely used for angina pectoris. Several recent case series have suggested that topical nitroglycerin also has promise for the treatment of chronic anal fissures (1, 2). The purported mechanism involves the donation of nitric oxide, which acts as an inhibitory neurotransmitter, thus reducing tone in the internal anal sphincter. This study by Lund and Scholefield is important because it is the first randomised, placebo-controlled trial of this drug for anal fissure.

The expected increase in anodermal blood flow and decrease in MARP were documented in this study at the time of first treatment. Whether tachyphylaxis occurred with time was not assessed; however, the clinical outcomes show a marked advantage in both pain scores and healing rates in the patients using GTN ointment compared with patients in the placebo group at 4-week follow-up. Headache occurred in more than half of the patients using GTN ointment but led to discontinuation of treatment in only 1 of these patients.

Chronic anal fissure is a relatively minor anatomical lesion, but it affects many people and can seriously impair quality of life to the point where some patients will accept the risk associated with sphincterotomy to get relief of symptoms. Topical glyceryl trinitrate appears to be an effective alternative treatment for chronic anal fissure. Whether it will replace sphincterotomy as a first-line therapy will need to be tested in a randomised controlled trial with sphincterotomy as the control treatment.

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References
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