

Original Article

GTN Ointment in the Treatment of Anal Fissures: Audit of Local Experience in Mubarak Al-Kabeer Hospital, Kuwait

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ABSTRACT

Objective: To evaluate the role of topical glyceryl trinitrate (GTN) ointment as a non-surgical treatment for anal fissure. Anal fissure is an ischemic disease caused by spasm of internal anal sphincter. Nitric oxide from GTN causes chemical sphincterotomy and improves blood flow, thus healing the anal fissure.

Design: Prospective study conducted from May 2003 to April 2004

Setting: Surgical outpatient clinic, Department of Surgery, Mubarak Al-Kabeer Hospital, Kuwait

Subjects: Eighty-six patients (42 male and 44 female) were recruited. Thirty seven patients had acute and 49 had chronic anal fissure.

Interventions: All patients were treated with topical 0.2% GTN ointment twice daily with additional application after defecation.

Main Outcome Measures: An independent observer

assessed the patients until full healing of fissures.

Results: Patient compliance was good. One patient developed transient mild headache. All patients achieved great reduction in pain score from a mean of 5.3 pre-treatment to 0.92 after one week and nearly zero at 4 - 6 weeks' treatment. Complete healing occurred at four weeks in all cases from the acute anal fissure group (100%) and in 37 patients (75.5%) from the chronic anal fissure group. Twelve (24.4%) unsuccessful patients with chronic anal fissure underwent surgical sphincterotomy. Recurrence occurred at two months in three patients (8.1%) with acute anal fissure requiring another course of GTN ointment, and in one patient (2.04%) with chronic anal fissure who required surgery.

Conclusion: GTN ointment for anal fissure should be considered as a first line treatment prior to surgical intervention in order to reduce complications of surgery.

KEYWORDS: anal fissure, first line treatment, GTN ointment

INTRODUCTION

Anal fissure is a common anal disease. Current theory suggests that the cause of healing failure is due to spasm of the internal sphincter which generates high pressure in the anal canal and leads to secondary local ischemia of the mucosa^[1-3].

Surgical lateral internal sphincterotomy is associated with troublesome incidence of minor form of anal incontinence (5.3 - 35.1%)^[4-7].

Nitric oxide (NO) has been shown to be an inhibitory neurotransmitter in the internal anal sphincter^[5,6,8]. Glyceryl trinitrate (GTN) ointment applied to the anus leads to a significant fall in maximum anal resting pressure (MARP) by 20-27% and an increase in anoderm blood flow, thus resulting in healing of the fissure^[3,9-11].

PATIENTS AND METHODS

Between May 2003 to April 2004, 86 patients with

anal fissure were prospectively studied. There were 42 male (48.8%) and 44 female (51.1%) subjects, with a mean age of 40 years (range 20 - 60 years). Acute anal fissure was seen in 37 (43.02%) and chronic anal fissure in 49 patients (56.9%). The site of anal fissures was posterior in 79 patients (92%), anterior in four women (4.6%) and both anterior and posterior in three women (3.4%)

All patients were treated with topical 0.2% GTN ointment twice daily with additional application after defecation. An independent observer assessed the patients and did the follow up was until full clinical healing of the anal fissure. Pain score (from 0-10), clinical examination, compliance and side affect of the treatment were recorded. Complete reduction of clinical symptoms and re-epithelialization of the lesion defined healing of the fissure. Patients with additional anorectal disease or prior anorectal surgery were excluded from this study.

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Table 1: Result of GTN treatment for acute and chronic anal fissure

	Acute Anal Fissure n (%)	Chronic Anal Fissure n (%)
Total number of patients	37	49
Healing at 6 weeks	37 (100)	37 (75.5)
Failure	-	12 (24.4)
Recurrence	3 (8.1)	1 (2.04)

RESULTS

A total of 86 patients were treated over the 12 months period with 0.2% topical GTN ointment. All were compliant with the topical GTN treatment as prescribed. There was great pain relief, as the mean pain score decreased from 5.3 in the pre-treatment period to 0.92 after one week of treatment and nearly to zero at 4 - 6 weeks treatment.

There was progressive epithelialization of the anal fissure with complete healing at four weeks in all cases of acute anal fissures and in 37 (75.5%) patients of chronic anal fissure. In the chronic anal fissure group, 12 patients (24.4%) failed to respond and underwent surgical lateral sphincterotomy.

Transient mild headache was reported by one patient (1.16%). However, this did not require discontinuing the treatment. None of our patients developed the potential side effect of GTN therapy such as hypotension, syncope, rebound hypertension, crescendo angina or allergic dermatitis.

At two months follow-up after full healing of the anal fissure there were three recurrences in the acute anal fissure group that were treated successfully with another course of GTN ointment. In the chronic anal fissure group there was one recurrence that required surgery (Table 1).

DISCUSSION

GTN belongs to the group of organic nitrates. Their action is derived from their metabolic conversion to nitric oxide in the vascular smooth muscle cells^[11]. It also plays an important role in nonadrenergic, noncholinergic nerve-mediated relaxation of gastrointestinal smooth muscle including the anal sphincter^[3,12]. Passive diffusion of GTN, a nitric oxide donor, through normal skin leads to therapeutic plasma level, mediating relaxation of the smooth muscle after a few minutes^[11].

Myenteric nerves innervating the internal sphincter muscle of the anus produce and release nitric oxide, mediating relaxation of this muscle^[13,14]. Derangement in the nitric oxide regulation may underlie the anal-sphincter hypertonicity associated with anal fissure and ulcer^[13].

From various studies, it was established that nitric oxide is the most important inhibitory neurotransmitter of the internal anal sphincter^[3,8,9,11,13,15,16]. GTN is one of the groups of organic nitrates that bind to protein receptors releasing nitric oxide. This leads to a fall in maximum anal resting pressure and increase in the anodermal blood flow. Interestingly, it was found that the patients who applied GTN reported a greater amelioration of pain than those using local anesthetic (lidocaine). This indicates the additional effect of GTN in improving vascular perfusion^[3,8,9,11,13,15,16].

Our results revealed great satisfaction of patients with the treatment, as it did not interfere with their life activities and avoided surgery. In addition, the healing rate with treatment was 75.5% with chronic anal fissure and 100% in acute anal fissure; this was associated with a low rate of side effects (1.16%, one patient). That patient developed a transient mild headache, which was self-limiting, did not interfere with the patient's daily activities and/or require discontinuation of GTN ointment treatment.

Nitroglycerin has been used as an antianginal agent since 1879; the adverse reactions were related to its activity as a vasodilator and were proportional to dosage^[17]. Although headache is the most common complication of nitrate therapy of coronary artery disease, other complications such as hypotension, syncope, rebound hypertension, crescendo angina or allergic dermatitis may occur. The relatively small dosages used in the treatment of anal fissures may be responsible for the low incidence of side effects^[18].

Resistant or insensitive internal anal sphincter to the endogenous nitric oxide, shorter duration of action of glyceryl trinitrate of less than eight hours and the development of tachyphylaxis (a previously effective dose becoming ineffective with time) are some of the possible reasons for failure GTN treatment for anal fissure^[19,20].

In our study, the use of GTN was associated with a great reduction in mean pain score from 5.3 to 0.92 after one week of treatment and nearly zero at four weeks. The failure rate was 12.94% in chronic anal fissure group. Those patients were treated with lateral sphincterotomy. Many studies have shown that GTN treatment failure for anal fissure was associated with failure of reduction of maximum anal resting pressure^[10].

CONCLUSION

Application of GTN ointment as a local treatment for anal fissure should be considered as first line treatment to reduce complications of surgery. However, it will not be able to obviate surgery in some patients with chronic anal fissure, but will still be able to reduce the rate of surgery in general.

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