CLINICAL ALERT

Botulinum toxin promoted healing and relieved symptoms of chronic anal fissure

Maria G, Cassetta E, Gui D, et al. **A comparison of botulinum toxin and saline for the treatment of chronic anal fissure.** *N Engl J Med* 1998 Jan 22;338:217-20.

Question

In patients with chronic anal fissures, is local infiltration of botulinum toxin effective for healing fissures and relieving symptoms?

Design

2 month randomised, double blind, placebo controlled trial.

Setting

Clinical centre in Rome, Italy.

Patients

30 patients (mean age 44 y, 67% men) with chronic, idiopathic anal fissures. Exclusion criteria were acute fissures, anal fissures with various causes (haemorrhoids, fistula in ano, or inflammatory bowel diseases), or previous anal surgery. Follow up was complete.

Intervention

Patients were allocated to 0.4 ml in 2 injections of either botulinum toxin A (Botox, Allergan, Irvine, CA, USA), 20 U (n=15), or saline placebo (n=15), injected with a 27 gauge needle. Patients were advised to eat food with a high fibre content and received a prescription for laxatives.

Main outcome measures

Anal fissure healing and symptomatic relief (persistence of anal fissure without symptoms). Patients were assessed at 1 and 2 months.

Main results

At 1 and 2 months, more patients allocated to botulinum toxin than to placebo had healed fissures ($p=0.05$ at 1 month and $p=0.003$ at 2 months) and symptomatic relief ($p=0.003$

for both 1 and 2 months follow up) (table). 4 patients who still had fissures were retreated with botulinum toxin, 25 U, and all achieved complete healing within 2 months of rescue treatment. No relapses occurred among patients in the botulinum toxin group during a mean follow up of 16 months. 10 patients in the control group received botulinum toxin, 20 U each, and 3 patients underwent sphincterotomy at 2 months. No relapses occurred after rescue treatment in the control group during a mean follow up of 18 months.

Conclusion

Botulinum toxin promoted healing and relieved symptoms of chronic anal fissure.

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Botulinum toxin v placebo for chronic anal fissure*

Outcomes	Botulinum toxin	Placebo	RBI (95% CI)	NNT (CI)
Healed fissure at 1 mo	53%	13%	300% (20 to 1415)	3 (2 to 17)
Healed fissure at 2 mo	73%	13%	450% (79 to 1913)	2 (1 to 4)
Symptomatic relief at 1 mo	87%	27%	225% (56 to 708)	2 (1 to 4)
Symptomatic relief at 2 mo	87%	27%	225% (56 to 708)	2 (1 to 4)

*RBI=the proportional increase in rates of good events between the botulinum toxin and placebo groups; NNT=the number of patients who must receive botulinum toxin to achieve 1 additional good outcome.

Commentary

Fissure is common, lying on the inside of the distal anal canal, usually posteriorly, but it is easily missed clinically unless traction is exerted on the rim of the anal canal. Local trauma by constipated stools leads to a tear; spasm and the resulting poor perfusion lead to an ischaemic ulcer which fails to heal.¹

Non-operative treatments such as laxatives and local anaesthetics try to break the pain/constipation cycle. In failures, surgical sphincterotomy reduces resting anal pressure, improves local blood flow and successfully heals the fissure, but at the price of (usually minor) incontinence in a few.

Resting anal pressure can also be reduced either by local application of a nitric oxide donor such as glyceryl trinitrate (GTN) or by injection of botulinum toxin A. Maria *et al* report a small randomised trial in 30 patients of 20 U botulinum toxin A versus saline (0.4 ml of each) injected into the internal anal sphincter in outpa-

tients with neither sedation nor anaesthetic. The treated patients were on average nine years younger and eight were women, compared with only two female controls. By two months, 73% of treated patients had healed compared with 13% of controls ($p=0.003$). After treatment of failures only six patients underwent surgery, all initially controls. By an average of 16 months follow up there had been no recurrences.

The alternative and probably equally effective new local therapy of 0.2% GTN cream needs to be diluted in soft paraffin wax in local pharmacies from the currently commercially available 2% cream.² Headache can be a problem. Bethanechol and diltiazem, alone or combined, are even newer options which work through different pathways without the side effects seen with GTN.³

Before surgeons are asked to hang up their scalpels for good, gastroenterologists

and general practitioners should be wary of future recurrences and know that other conditions, familiar to surgeons, mimic or even open into fissures. Furthermore, patient satisfaction with surgical sphincterotomy generally remains high.

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1 Schouten WR, Briel JW, Auwerda JJ. Relationship between anal pressure and anodermal blood flow: vascular pathogenesis of anal fissures. *Dis Colon Rectum* 1994;37:664-9.

2 Lund JN, Scholefield JH. A randomised, prospective, double blind, placebo-controlled trial of glyceryl trinitrate ointment in treatment of anal fissure. *Lancet* 1997;349:11-14.

3 Carapeti EA, Kamm MA, Phillips RKS. Diltiazem lowers resting anal sphincter pressure - a potential low side effect alternative to glyceryl trinitrate for fissures. *Gut* 1998; 42(suppl 1):A97.