original paper

Efficacy of botulinum toxin in chronic anal fissure

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Abstract

Background Chronic anal fissures (CAF) are caused by anal sphincter hypertonia leading to an ischaemic ulcer. By inducing temporary sphincter relaxation, botulinum toxin (Botox) injection has been shown to heal CAF in approximately 73-96% of cases in clinical trials.

Aim This study looks at the efficacy of Botox clinical practice.

Methods The medical charts were reviewed of all patients with CAF treated with Botox (30iu injected into the sphincter complex in three 10iu aliquots) in the Ulster Hospital, Dundonald, Northern Ireland between March 1999 and November 2001.

Results Fifty-one charts were identified. Four patients failed to attend for review and were excluded from the study. Of the remaining 47 patients, 37 (78.7%) were healed following Botox injection. 10 out of 37 (27.0%) developed a recurrent CAF after a median time of 16.0 months (IQR 3.8-20 months). Eight of these patients opted for repeat Botox injection, which was successful in 7 (87.5%) cases. No adverse effects were reported.

Conclusion Botox injection for the treatment of CAF is as effective in clinical practice as reported in clinical trials from specialist centres.

Introduction

An anal fissure is a tear of the mucosa extending from the anal verge towards the dentate line. It is a common condition, affecting 10% of patients attending proctology clinics[1] and usually presenting with pain and small amounts of bright red rectal bleeding. Fissures lasting greater than two months with features of chronicity (sentinel skin tag, hypertrophied anal papilla, exposure of the underlying internal anal sphincter [IAS] or anal cicatrisation) are unlikely to heal with conservative management and are categorised as chronic anal fissures (CAF).

CAF can be considered an ischaemic ulcer of the anal mucosa due to IAS hypertonia. The maximum resting anal pressure (MRAP) in patients with CAF is usually greater than 90 mmHg,[2] causing compression of the end-arteries (mean arteriolar blood pressure 85mmHg) which pass through the IAS to reach the posterior commisure.[3] This causes a reduction in the posterior anodermal blood flow which can be measured using laser Doppler flowmetry.[4] This explains why surgery disrupting the IAS hypertonia improves anodermal blood flow and allows the fissure to heal. Although highly effective, lateral internal sphincterotomy (LIS) carries a 0.4-4.9% risk of faecal incontinence.[5,6]

Current pharmacological treatments causing temporary sphincter hypotonia (chemical sphincterotomy) vary in their efficacy, side-effects and cost. They include topical nitric oxide donors (e.g. glyceryl trinitrate-[GTN]), topical calcium antagonists (e.g. nifedipine) and injection of the neurotoxin botulinum toxin (Botox). A prospective randomised trial has shown that Botox injection is superior to GTN in the treatment of CAF.[7] At two months, the healing rate in the Botox group was significantly higher than that of the GTN group (96% vs 60% respectively).

Botox has been used in the authors' unit for three years. The current study was undertaken to evaluate the efficacy of Botox therapy in the treatment of CAF in clinical practice, outside the setting of a clinical trial.

Methods

All patients receiving Botox treatment of a CAF from 26 March 1999 to 30 November 2001 were identified from the theatre ledgers. They were under the care of four consultants with an interest in colorectal surgery. The medical records of all patients identified were reviewed. Clinical and demographic details were recorded. The previous use of alternative treatments was also recorded.

In all cases, 30iu of Botox was diluted in 1ml of 0.9% saline and injected in three 10 iu aliquots into the anal sphincter complex. This was performed as a day-case procedure under either sedation or general anaesthesia, especially if performing an examination of the rectum at the same time to exclude any further pathological process. All patients were given a review appointment six to eight weeks after the procedure.

Results

Patients

Fifty-one charts were identified where Botox had been used for the treatment of CAF, four did not attend for review and were excluded from further analysis. The clinical details of the remaining 47 patients are summarised in Table 1. The median time from first Botox injection to chart review (follow-up period) was 12.6 months (IQR 8.9-18.9 months).

There was a 78.7% (37/47) success rate following Botox injection with a 27% (10/37) recurrence rate. One of the successfully treated patients was a 69-year-old male with Crohn's disease who had a 12-month history of a posterior CAF previously unresponsive to topical 0.2% GTN ointment.

Topical 0.2% GTN ointment applied twice daily had been used prior to Botox injection in 68% (32/47) of cases in this study. It was of no benefit in 75% (24/32) of cases, was not tolerated in 12.5% of cases due to headaches and was of only temporary benefit in 12.5% cases. Where GTN had been of no benefit, 19 were successfully treated with Botox with a

Table 1. Characteristics of patients with chronic anal fissures receiving Botox

	Age (years)	Female (n)	Symptoms duration (months)	Site (n)* Posterior	Anterior	Anterior+ Posterior	Symptoms (n)** Pain	Bleeding	Pain +bleeding
Successful (n=37)	46.2±4.8	21	10.0 (5.0, 18.0)	22	11	1	13	2	19
Unsuccessful (n=10)	44.9±2.4	4	10.0 (4.8, 12.0)	7	1		3		7

Age is summarised as mean±sem. Duration of symptoms is summarised as median (interquartile range).
*Data missing in five cases. **Data missing in three cases.

recurrence rate of 36.8% (7/19).

Of the ten primary Botox treatment failures, three were treated successfully with LIS, one with topical 0.2% nifedipine paste and four with topical 0.2% GTN ointment. One of the latter four patients had not responded to topical GTN prior to their failed Botox injection. The remaining two treatment failures have been treated with topical GTN and are awaiting review. None of these patients were offered a second Botox injection.

Recurrences following initial successful outcome (27%) occurred after a median time of 16.0 months (IQR 3.8-20 months). When further treatment options were discussed, eight patients opted for repeat Botox injection and two for LIS. The repeat Botox injection was successful in seven of eight cases. The eighth patient subsequently underwent an LIS. All three sphincterotomies were successful.

Using logistic regression, the likelihood of Botox injection being successful and the risk of subsequent fissure recurrence were both found to be independent of fissure site, duration/type of symptoms, age, sex or previous GTN treatment (whatever its outcome); $p>0.150$ for all variables. At review, none of the patients in the current audit reported incontinence.

Discussion

This study confirms the clinical efficacy of Botox therapy in the treatment of CAF. It produced fissure healing in 78.7% of cases with a recurrence rate of 27%. When reapplied following recurrence, the success rate was 87.5%. None of the initial treatment failures were treated with a second Botox injection and therefore it is not possible to comment on its use in such cases.

LIS was the treatment of choice for CAF prior to the introduction of temporary chemical sphincterotomy.[8] The five year failure rate following LIS is 2.3-3.0% with incontinence for flatus occurring in up to 36%, soiling in up to 21% and faecal incontinence in up to 5%.[5,6] Anal dilatation results in successful healing comparable to LIS.[9] However, post-operatively 65% have been shown to have sphincter damage on endoanal ultrasound[10] and one study has suggested a five-fold increase in the risk of incontinence following anal dilatation compared to LIS.[11]Topical GTN has been shown to heal CAF in up to 68% of cases[12-14] whereas Botox has a healing rate of 73-79% (100% with second injection) with up to an 8% recurrence rate.[15,16] GTN causes temporary incontinence of flatus in up to 13% of cases and mild headaches in up to 72%. Botox causes temporary incontinence of flatus in up to 7% and incontinence of stool in up to 2% of cases. A randomised trial comparing GTN and Botox found Botox to be more effective.[7] Fifty patients were prospectively randomised to receive Botox (20iu) or 0.2% GTN ointment applied twice daily for six weeks. At two months, the healing rate was significantly higher in the Botox group compared to the GTN group (96 vs 60%). Apart from one patient who underwent LIS following severe headaches whilst using GTN, the remaining failures were successfully treated after crossing over to the other treatment. No relapses were documented after an average follow-up of 15 months. This is in marked contrast to the current study where there was a 27% recurrence rate following Botox injection (30iu) within a median of 16.0 months (IQR 3.8-20 months).

Compared to GTN, Botox has a higher healing rate and abolishes the need for patient compliance. It is however expensive (£120/vial of 100iu), is not currently licensed for the treatment of CAF in the UK and temporary incontinence has been reported with its use. Although it can be injected in the outpatient clinic, this is uncomfortable and the authors administer Botox at the time of an examination of rectum under sedation or general anaesthesia. Careful planning of day-procedure lists can reduce the cost of Botox treatment by using a single vial to treat three patients on one list.

This study has shown that the efficacy of Botox in the treatment of CAF in clinical practice is similar to that reported in clinical trials, although the recurrence rate may be higher. Such recurrences can be effectively treated by a second Botox injection. As topical GTN is cheap the authors recommend it for the first line treatment of CAF which should be prescribed by the general practitioner. Patients unresponsive to topical GTN should be referred for Botox injection. All initial treatment failures and recurrences should be treated with a second attempt at chemical sphincterotomy. Surgical intervention should be reserved for patients in whom pharmacological treatment has failed or is not tolerated, as the risk of faecal incontinence can be unacceptably high.

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