Original article

Chronic anal fissures treated with botulinum toxin injections: a dose-finding study with Dysport®

W. H. Jost and B. Schrank

Department of Neurology and Clininical Neurophysiology, Deutsche Klinik für Diagnostik, Wiesbaden, Germany

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Summary

Botox® injection of the anal sphincter muscle cures chronic uncomplicated anal fissures in up to 80% of patients. This study examines the therapeutic efficacy and side effect profile of the British botulinum product Dysport®. Fifty patients (29 women) were recruited to participate in this randomized dose-finding study, their mean age being 32.9 years. The low dose group A was treated with a total dose of 20 U injected in two sites each lateral to the fissure, the high dose group B was treated with 40 U. Eighty-two percent of patients were pain-free within a week following the injections. The fissure was healed in 78% of treated patients after 3 months. Three patients relapsed within 6 months. The most common adverse side effect was transient incontinence ($n = 4$). Clinical outcome was not significantly different between the two treatment groups. The low dose can therefore be regarded sufficient for the treatment of anal fissure. Therapeutic efficacy was equivalent to published data on Botox treatment. Both Dysport® and Botox® can therefore be used to treat chronic uncomplicated anal fissures. Both Dysport® and Botox® therapy are well tolerated, can be performed on an out-patient basis and avoid the risk of permanent faecal incontinence which complicates surgical treatment of anal fissures.

Keywords Botulinum toxin, anal fissure, anal sphincters

Introduction

Following our suggestion to inject botulinum toxin (BoTx) into the external anal sphincter for the treatment of anal fissure in 1989, we have standardized this form of treatment [1,2] and others have confirmed our results [3–6]. In one of our recent papers we were able to demonstrate excellent results in 100 patients treated with the American product Botox® over a 6-month follow-up period [7]. So far, no data have been published on the efficacy of the British botulinum product Dysport®.

For standard indications of botulinum toxin treatment comparable results can be achieved with both Dysport® and Botox®, although neither the exact dose equivalent nor the diffusion characteristics have been defined for the two products. In both products the active substance is botulinum toxin A, which inhibits acetylcholine release into the synaptic gap. The resulting muscle weakness of the injected muscle may persist for weeks. The toxin was first used in proctology by the British surgeon Hallan for the treatment of anismus [8].

Correspondence to: Priv. Doz. Dr. med. Wolfgang H. Jost, Department of Neurology, Deutsche Klinik für Diagnostik, Aukammallee 33, D-65191 Wiesbaden, Germany.

Patients and methods

In the current study we examined the influence of Dysport® injections on healing of chronic anal fissure. The trial was conducted as a randomized dose-finding study.

Criteria for inclusion in the study were disease duration of at least 3 months, absence of severe secondary changes, uncomplicated fissure in the posterior or anterior midline, increased sphincter tone (pressure at rest > 100 mmHg, determined by manometry using a Synectics Medical device, normal values defined according to control measurements from our own laboratory), and failure of conservative treatment of at least 2 months duration (supervised by the referring surgeon). All patients were offered sphincterotomy or fissurectomy as an alternative form of treatment.

Criteria for exclusion were pregnancy, fistula, distinct secondary changes, i.e. cicatricial alterations, large sentinel pile, subfissural infiltration, increased tendency to bleeding, anti-coagulative therapy, and age <18 years or >70 years.

Fifty patients were recruited to participate in the study (29 female, 21 male), their average age being 32.9 years

(18–57 years). The mean duration of fissure-related complaints was 12.8 months. The patients were fully informed about the mode of action and adverse side effects of Dysport® and gave their informed consent.

Following randomization, in patients of group A the anal sphincter was injected in two sites just lateral to the fissure margins, each injection containing 0.1 ml diluted toxin corresponding to 10 U Dysport® (Ipsen Pharmaceuticals). In group B 20 U Dysport were injected into the same sites adjacent to the fissure margins. For injection we used an insulin syringe with a short and thin needle (27 G).

Results

We re-examined all patients 1 week and 3 months following the injection procedure. Forty-one of the 50 patients (82%) reported to have become pain-free within the first few days following the injection (Table 1). At week 1 post-injection 47 patients showed a markedly reduced external sphincter tone. In three patients from group B the tone of the puborectalis sling was decreased. In all patients digital examination was possible without causing pain. Three patients complained about incontinence for flatus for <2 weeks, two of them suffered from faecal incontinence for about 1 week. No severe adverse effects, such as infections or systemic side effects, were observed.

Three months after injection therapy the fissure had healed completely in 39 cases (19 patients in group A, 20 patients in group B). These patients stated that they were asymptomatic. Their sphincter tone was within normal limits and no incontinence occurred. A relapse was seen in three cases within the 3 months (one patient in group A, two patients in group B).

There was no significant difference in healing rate between both groups, but a higher incidence of decreased sphincter tone of the puborectalis muscle in the group on a higher dosage, and therefore a higher incidence of transient incontinence.

Discussion

The introduction of BoTx injections into the anal sphincter muscle [1,2] and the local application of nitroglycerin ointment [9–11] have diversified non-surgical treatment options for anal fissures. In most patients anal

Table 1 Clinical and side-effect profile after Dysport® injection: low-dose group patients received 2 × 10 U (n = 25), high-dose group patients received 2 × 20 U (n = 25).

Time point after Dysport® injection	1 week		3 months	
Dosage group	Low dose	High dose	Low dose	High dose
Healing without surgery	–	–	19/25	20/25
Relapse within study period	–	–	1/25	2/25
Resolution of pain	20/25	21/25	19/19*	20/20*
Reduced sphincter tone	22/25	25/25	0/19*	0/20*
Reduced puborectal muscle tone	0/25	3/25	0/19*	0/20*
Transient incontinence	1/25	3/25	0/19*	0/20*

* Results in patients with healed fissure.

Table 2 Botox® and Dysport®: historical comparison of therapeutic efficacy and side effect profile [1,2].

Time point after Botox injection	1 week		3 months	
Product used	Botox®	Dysport®	Botox®	Dysport®
Healing without surgery	–	–	82%	78%
Relapse	–	–	5%	6%
Resolution of pain	78%	82%	41/41*	39/39*
Reduced sphincter tone	89%	94%	0	0
Reduced puborectal muscle tone	4%	6%	0	0
Transient incontinence	7%	8%	0/41*	0/39*

* Results in patients with healed fissure.

fissures can now be managed conservatively. The success rate for low dose BoTx injections is 70–80%. The incidence of adverse side effects is very low. We observed transient mild faecal incontinence only. According to our data, there is no significant difference in therapeutic efficacy between the American Botox® and the British Dysport® (Table 2). Our data show that the low-dose treatment (2×10 U Dysport®) is as effective as higher doses and is therefore preferred because of a lower incidence of faecal incontinence. As the toxin will also diffuse into the internal anal sphincter muscle we inject the external sphincter only. Regardless of whether internal or external sphincters are injected, both muscles will become paretic. Injection into the external sphincter muscle produces better results, as it is technically easier to perform. In addition, our data suggest that the external anal sphincter is a major contributor to the pathologically increased sphincter tone implied in the pathogenesis of anal fissures [12].

Botulinum toxin is an ideal agent to break the vicious circle of inflammation, pain, and sphincter spasm for a time period sufficient to allow healing of the fissure, especially in uncomplicated anal fissures when conservative treatment does not lead to healing. The topical application of nitroglycerin is an established alternative approach [9–11]. The main reason for failure of topical nitroglycerin is poor patient compliance, as many patients will only apply the ointment when recurrence of local pain reminds them of their problem, thus promoting a chronic fissure. With BoTx treatment surgical measures like fissurectomy are only required in fissures complicated by distinct secondary changes.

Lateral anal sphincterotomy is still the current therapy of choice in anal fissure [13–15], but this may change within the next few years. In our opinion BoTx is preferable to lateral sphincterotomy, because there is no damage of the continence organ and, correspondingly, no risk of permanent incontinence. Dysport® can be used as well as Botox®, and the dosage should be minimized (with Dysport® 20 U) to prevent transient incontinence.

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