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Kennedy Institute of Rheumatology, Hammersmith, London W6 7DW, and Academic Department of Rheumatology, Charing Cross and Westminster Medical School, London, UK; (M J Elliott PhD, Prof R N Maini FRCP, Prof M Feldmann PhD, A Long-Fox RGN, P Charles FIBMS); **and Centocor Inc, Malvern, Pennsylvania, USA** (J A Bijl MD, J N Woody MD)

Correspondence to: Prof Ravinder N Maini

Botulinum toxin for chronic anal fissure

D Gui, E Cassetta, G Anastasio, A R Bentivoglio, G Maria, A Albanese

Botulinum toxin can chemically denervate striated muscle. Botulinum toxin A (15 U) was used to treat ten patients with chronic anal fissure by injection in the internal sphincter. In seven patients, the lesion healed at 2 months after treatment; one relapsed at 3 months. In one patient the lesion healed at 1 month, but partly relapsed a month later. Mild faecal incontinence lasting for 1 day was observed in one patient. We propose that botulinum toxin injections in the internal anal sphincter be considered an alternative approach to surgical therapy of anal fissure.

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Unlike the acute fissure, chronic anal fissure is not usually self-limiting[1] and its pathophysiology is not completely understood.[2] Hypertonicity of the internal anal sphincter may be involved.[3] The recommended treatments are anal dilation or lateral internal sphincterotomy, which are successful in 85–95% of patients. Internal sphincterotomy permanently weakens the sphincter, which may be associated with incontinence, infection, and anal deformity.[4]

Chemical denervation with botulinum toxin is a versatile tool for targeted weakening of striated muscles.[5,6] The toxin may also weaken smooth muscle in the gastrointestinal tract.[7] We have evaluated local injections of botulinum toxin to reduce hypertonus of the internal anal sphincter and induce healing in patients with idiopathic anal fissure.

Ten consecutive outpatients (mean age 42·4, range 24–82) with chronic idiopathic anal fissure gave informed written consent for study (table). They had had symptoms for a mean of 13·65 (SE 3·52) months. All had typical features of chronic anal fissure: posterior anal fissure, with a large sentinel tag of skin and the exposure of fibres of the internal sphincter; and post-defaecatory pain for over 2 hours. No patient had nocturnal pain. All patients were advised to eat food with high-fibre content and received a prescription for laxatives. No patient was treated with topical anaesthetic agents before or during study.

Anal manometry at rest and after maximum voluntary contraction was done before treatment and at each follow-up. The normal range for our laboratory is 66 (23) and 144 (60) mm Hg, respectively.[8] Type A botulinum toxin (Botox, Allergan) was diluted in saline to 50 U/mL. The anal sphincter was easily palpated and injected with a 27 G needle. Every patient received three injections of 5 U (0·1 mL) each within the contracted muscle; two injection sites were located laterally, the other posteriorly. No anaesthesia was used during the 5 minute procedure. The patients were evaluated 1 week, 1 month, and 2 months after treatment by anoscopy, anal manometry, and a clinical evaluation. At each visit the patients were asked whether, despite any local pain, they wanted to stay in the study. If not, they were offered anal sphincterotomy.

Efficacy (strength of internal and external anal sphincters) was evaluated by multifactorial analysis of variance, by comparison of resting anal pressure or maximum voluntary pressure before treatment with post-injection values. The time course of variations in the two pressures was analysed by *t* test.

1 week after treatment, all patients still had fissure. Post-defaecatory pain had disappeared in five patients and reduced in four. Pain during exploration had disappeared in five and was reduced in the others. Compared with baseline, resting pressure was reduced by 25·2% ($p<0·05$). Maximum voluntary pressure, although lower on average, did not differ statistically from baseline (table).

Inspection at 1 month after treatment revealed a healing scar in six patients. Compared with pretreatment records, post-defaecatory pain had disappeared in seven patients and was reduced in one; pain during exploration had disappeared in six and was lower in one. Compared with baseline, resting pressure was reduced by 23·9% ($p<0·05$), whilst voluntary pressure was unchanged. The two pressures were not significantly different from 1 week values.

At 2 months, seven patients had a healing scar. The fissure was observed again in patient 5, who had had a healing scar at 1 month. Her subjective symptoms, however, were mild. Compared with pretreatment, post-defaecatory pain had disappeared in seven patients and was

Patient (age/sex)	Duration (mo)	Inspection			Outcome	Resting pressure (mm Hg)				Maximum voluntary pressure (mm Hg)			
		1 wk	1 mo	2 mo		Baseline	1 wk	1 mo	2 mo	Baseline	1 wk	1 mo	2 mo
1 (24/F)	9	Fissure	Healing	Healing	Healing	90	60	50	50	75	65	40	50
2 (43/F)	12	Fissure	Healing	Healing	Healing	85	80	50	75	45	30	25	20
3 (43/F)	36	Fissure	Fissure	Fissure	Ineffective	85	50	80	80	60	25	60	60
4 (25/M)	1·5	Fissure	Fissure	Healing	Healing	75	65	50	85	50	25	40	100
5 (45/F)	18	Fissure	Healing	Fissure	Relapse	60	50	40	85	25	12	15	25
6 (27/M)	12	Fissure	Healing	Healing	Relapse	80	75	75	90	50	90	90	100
7 (50/M)	20	Fissure	Healing	Healing	Healing	80	60	40	40	85	85	100	100
8 (28/M)	24	Fissure	Healing	Healing	Healing	60	45	50	70	100	50	100	100
9 (82/F)	3	Fissure	Fissure	Fissure	Ineffective	95	45	100	100	20	10	30	30
10 (57/F)	1	Fissure	Fissure	Healing	Healing	65	50	55	40	20	25	30	25
Mean (SE)	..	..	..	..	..	77·5 (3·89)	58 (3·89)	59 (6·18)	71·5 (6·71)	53 (8·69)	41·7 (9·24)	53·5 (10·03)	61 (11·27)

Table: **Clinical outcome, and manometry**

lessened in two; pain during exploration had disappeared in five and was lower in three. Resting and voluntary pressures did not differ significantly from baseline or from values recorded 1 week and 1 month after treatment.

Analysis of baseline resting pressure and values after treatment revealed that the internal anal sphincter had been significantly weakened ($p < 0.05$). No variations occurred at different times after treatment, indicating that the effect of the toxin had not worn off at 2 months. On the contrary, there was no effect on maximum voluntary pressure, indicating a lack of effect on the external anal sphincter.

All the patients were re-evaluated in May, 1994. No relapse had occurred in patients 8 and 10, 2 months after treatment, in patient 7 at 3 months, and in patients 1 and 2 at 6 months. Patient 4 had some subjective symptoms, but no relapse, at 4 months after. Patients 3, 5, and 9 were re-treated with botulinum toxin with the same regimen. Patient 3 requested surgical sphincterotomy soon after the second treatment; patients 5 and 9 reported subjective benefit a few days after their original treatment. Patient 6 relapsed 3 months after the treatment; he was retreated with botulinum toxin (a total of 20 U in two sites) and had a complete healing. The patients who had a relapse of fissure reported that subjective symptoms were milder than before treatment.

No complications were reported during injection or follow-up. Patient 5 had a transient mild faecal incontinence for about a day 1 month after treatment. No other side-effects occurred.

We have shown that botulinum toxin can be used to treat chronic idiopathic anal fissure by injecting the internal anal sphincter. The lesion healed in eight of ten patients. Two healed patients relapsed. Thus, long-lasting healing of the lesion occurred in six cases.

Resting anal pressure decreased after treatment, whereas treatment for maximum voluntary pressure was unaffected. Since resting anal pressure depends on the activity of the external sphincter, it appears that botulinum toxin weakens the internal sphincter. Thus the botulinum toxin did not diffuse to the external sphincter when low doses were distributed in the internal sphincter. Resting pressure tended to rise by 2 months after treatment, indicating that muscle weakening tended to disappear with time.

Chronic anal fissure is maintained by contraction of the internal anal sphincter, triggered by the excruciating pain.[9] Botulinum toxin may interfere with such a vicious circle by temporarily weakening the internal sphincter. Increased sphincter tone may reduce blood supply to the posterior anal canal by compressing the vessels passing vertically through muscle fibres.[10] If this is a contributing pathogenic cause for anal fissure, it would be positively affected by chemical denervation.

Because of the low frequency of side-effects and the lack of complications, higher doses of botulinum toxin might be used either as first treatment or for retreatments. In addition, injections could be done posteriorly, close to the fissure, to weaken muscle fibres travelling near the inferior rectal artery.

Chemical denervation produced by the toxin is not permanent; clinical efficacy lasts for 2–3 months.[5,6] In patients with dyskinesias, repeated treatments are required to obtain sustained action; this affects compliance and increases costs. In anal fissure, however, the duration of action of the toxin roughly corresponds to the time required to reduce the hypertonus of the internal sphincter and allow for a healing. Thus botulinum toxin may represent a tool for testing some current hypotheses on the pathophysiology of anal fissure. In addition, at variance with all the other known indications of this toxin, chemical denervation of the internal sphincter may constitute a pathogenic rather than a symptomatic approach for chronic anal fissure.

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Istituto di Clinica Chirurgica (D Gui MD, G Anastasio MD, G Maria MD) **and Istituto di Neurologia** (E Cassetta MD, A R Bentivoglio MD, A Albanese MD), **Università Cattolica del Sacro Cuore, I-00168 Roma, Italy**

Correspondence to: Dr Alberto Albanese