

# Bilateral versus posterior injection of botulinum toxin in the internal anal sphincter for the treatment of acute anal fissure

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*Aim.* Comparison of bilateral versus posterior injection of botulinum toxin into the internal anal sphincter for treatment of acute anal fissure.

*Methods.* Forty patients with acute anal fissure were randomly divided into two equal groups. Group 1 was treated by injecting 20 units of botulinum toxin into each side of the internal anal sphincter, and group 2 by injecting 25 units of botulinum toxin into the midline posteriorly.

*Results.* The mean time to pain relief was 8.45 (standard deviation (SD) 7.41) days in group 1 and 7.20 (SD 7.19) days in group 2. Healing took place in a mean of 5.20 (SD 1.85) weeks in group 1 and 5.40 (SD 2.01) weeks in group 2. Fissures failed to heal in 2 patients in group 1 and 3 in group 2, and recurred in 4 patients in group 1 and 3 in group 2.

*Conclusion.* Botulinum toxin injection is effective in treating acute anal fissure. A single posterior injection is easier and less painful than bilateral injection, and is as effective in pain relief.

Anal fissure is a common, painful condition that causes significant morbidity, mostly in young adults.<sup>1</sup>

Acute anal fissures often heal spontaneously or with the help of medical treatment. Recurrence rates range from 30% to 70% if treatment is abandoned after the fissure is healed.<sup>2</sup>

The aim of this study was to compare two sites of injection of botulinum toxin, bilateral versus posterior.

## Patients and methods

The study was carried out in the Department of General Surgery, Ghodran General Hospital, Kingdom of Saudi Arabia, during the period October 2005 - February 2008. Forty patients with acute posterior anal fissure were randomly divided into two equal groups using a computer randomisation program ([www.randomization.com](http://www.randomization.com)). Patients with other anal pathology (i.e. inflammatory bowel disease, haemorrhoids, anal fistula or anal abscess) were excluded from the study. All patients received a full explanation of the proposed procedure and gave informed consent. The study protocol was approved by the Ethics Committee of Ghodran General Hospital.

All patients were diagnosed as having acute anal fissure on the basis of their medical history and the findings on physical examination. Pain was evaluated using a visual analogue scale<sup>3</sup> before treatment. All the patients were treated by the same surgeon on an outpatient basis.

Hundred-unit vials of type A lyophilised botulinum toxin (Botox, Allergan Inc., Irvine, CA, USA) were diluted in saline to a concentration of 50 U/ml immediately before injection. Patients in group 1 were treated by injection of botulinum toxin into each side of the internal sphincter with a 25G needle, under direct vision and guided by digital examination (a total of 40 U per patient). No sedation or local anaesthesia was used during the procedure.

Group 2 patients received a single injection of 25 U botulinum toxin into the posterior midline of the internal sphincter with a 25G needle, under direct vision and using digital examination. No sedation or local anaesthesia was used.

Pain was evaluated daily by the patients at home, using a visual analogue scale. Our aim was complete pain relief and healing, defined as complete re-epithelisation of the fissure and absence of symptoms. A fissure was considered to have recurred if found on examination, whether it caused symptoms or not.

All patients were followed up by visits at 2-week intervals for 8 weeks then monthly for 6 months. After this, telephonic follow-up was done every 2 months until at least 1 year's follow-up was completed. The mean length of follow-up was 15.2 (standard deviation (SD) 4.3) months. Patients were asked about the presence or absence of pain and bleeding on defecation. The anus was examined visually to assess healing of the fissure.

Quantitative variables were expressed as means (SD). Qualitative variables were expressed as frequencies and percentages. Quantitative parametric variables were compared between the two groups using the unpaired Student's *t*-test, and quantitative non-parametric variables were compared using the Mann-Whitney test. Qualitative variables were compared using the chi-square test or Fisher's exact test (when the criteria for using the chi-square test were not sufficient). The power used was 0.80 and the level of significance was 5%.

## Results

Forty patients were included in the study, 23 females and 17 males. The ages of the patients ranged from 16 to 83 years, with a mean of 36.85 (SD 17.35) years. Pain on defecation was the main presenting symptom in all patients (Table I).

### Time to pain relief

In group 1 pain relief was achieved in a mean of 8.45 (SD 7.41) days, and in group 2 in a mean of 7.20 (SD 7.19) days. The difference between the two groups was not statistically significant (Table II).

### Time to complete healing

The mean time to healing was 5.20 (SD 1.85) weeks in group 1 and 5.40 (SD 2.01) weeks in group 2. The difference between the two groups was not statistically significant (Table III).

### Complications

Haematoma after injection occurred in 2 patients in each group, and the fissure failed to heal in 2 patients in group 1

and 3 in group 2. The differences between the two groups were not statistically significant.

### Recurrence

The fissure recurred in 4 patients in group 1 and 3 patients in group 2 (in 2 patients in group 1 and 2 in group 2 within 6 months after injection; in 1 patient in group 1 within 9 months after injection; and in 1 patient in each group within 12 months after injection). A second botulinum injection achieved healing in 3 patients, and the rest requested operative treatment and were referred for lateral internal sphincterotomy. The differences between the two groups were not statistically significant (Table IV).

### Discussion

Botulinum toxin causes denervation of the internal anal sphincter by preventing the release of acetylcholine from presynaptic nerve terminals.<sup>4</sup> Paralysis occurs within a few hours, but the transmission of neuromuscular impulses resumes after the growth of new axon terminals. Temporary weakness of the internal anal sphincter is experienced, lasting 3 - 4 months.<sup>5</sup> Studies of chronic anal fissure demonstrated a healing rate ranging from 60% to 76% after a single injection of 15 or 20 U botulinum toxin into the internal anal sphincter.<sup>6</sup> Sajid *et al.*<sup>7</sup> recommended chemical sphincterotomy with botulinum toxin as first-line therapy for chronic anal fissure. A study on patients treated with 15 or 20 U botulinum toxin showed that the higher dose was more effective than the lower dose with respect to long-term healing and was not associated with a higher rate of complications.<sup>8</sup>

We found a single injection posterior to the fissure to be easier and less painful than bilateral injection and to be as effective in pain relief. Use of a single injection did not decrease the efficacy of treatment. Increasing the dose of the injection did not lead to any adverse effects, but reduction of the total injected dose per patient was advantageous.

We conclude that injection of botulinum toxin into the

**TABLE I. CLINICAL DATA ON PATIENTS**

<b>Age (yrs)</b>	<b>Range 16 - 83, mean 36.85 (SD 17.35)</b>
<b>Gender</b>	
<b>Females</b>	<b>23 (57.5%)</b>
<b>Males</b>	<b>17 (42.5%)</b>
<b>Presentation</b>	
<b>Pain</b>	<b>40 (100%)</b>
<b>Constipation</b>	<b>34 (85.0%)</b>
<b>Bleeding</b>	<b>26 (65.0%)</b>
<b>Pruritus</b>	<b>9 (22.5%)</b>
<b>Total</b>	<b>40 (100%)</b>

**TABLE II. TIME TO PAIN RELIEF**

Time to pain relief	Group 1	Group 2	p-value
<b>First bowel movement</b>	<b>5 (25.0%)</b>	<b>7 (35.0%)</b>	<b>&gt;0.05</b>
<b>2 weeks</b>	<b>12 (60.0%)</b>	<b>12 (60.0%)</b>	<b>&gt;0.05</b>
<b>3 weeks</b>	<b>2 (10.0%)</b>	<b>0</b>	<b>&gt;0.05</b>
<b>4 weeks</b>	<b>1 (5.0%)</b>	<b>1 (5.0%)</b>	<b>&gt;0.05</b>
<b>Mean period to pain relief</b>	<b>8.45 (SD 7.41) days</b>	<b>7.20 (SD 7.19) days</b>	<b>&gt;0.05</b>

**TABLE III. TIME TO COMPLETE HEALING**

Time of healing	Group 1	Group 2	p-value
<b>2 weeks</b>	<b>0</b>	<b>0</b>	
<b>4 weeks</b>	<b>13 (65.0%)</b>	<b>12 (60.0%)</b>	<b>&gt;0.05</b>
<b>6 weeks</b>	<b>3 (15.0%)</b>	<b>3 (15.0%)</b>	<b>&gt;0.05</b>
<b>8 weeks</b>	<b>2 (10.0%)</b>	<b>2 (10.0%)</b>	<b>&gt;0.05</b>
<b>No healing</b>	<b>2 (10.0%)</b>	<b>3 (15.0%)</b>	<b>&gt;0.05</b>
<b>Mean time to healing</b>	<b>5.20 (SD 1.85) weeks</b>	<b>5.40 (SD 2.01) weeks</b>	<b>&gt;0.05</b>

**TABLE IV. TIME TO RECURRENCE**

Time to recurrence	Group 1	Group 2	p-value
<b>3 months</b>	<b>0</b>	<b>0</b>	<b>&gt;0.05</b>
<b>6 months</b>	<b>2 (10.0%)</b>	<b>2 (10.0%)</b>	<b>&gt;0.05</b>
<b>9 months</b>	<b>1 (5.0%)</b>	<b>0</b>	<b>&gt;0.05</b>
<b>12 months</b>	<b>1 (5.0%)</b>	<b>1 (5.0%)</b>	<b>&gt;0.05</b>
<b>Total</b>	<b>4 (20.0%)</b>	<b>3 (15.0%)</b>	<b>&gt;0.05</b>

internal anal sphincter is effective in treating acute anal fissure and in preventing its chronicity. A single posterior injection is easier and less painful than bilateral injection and as effective in pain relief. It does not decrease the efficacy of treatment but reduces the total injected dose per patient.

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