

Botulinum toxin injection versus internal anal sphincterotomy for the treatment of chronic anal fissure

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BACKGROUND: Anal fissure is a chronic condition characterized by painful defecation and rectal bleeding. The aim of this study was to compare injection of botulinum toxin versus surgical sphincterotomy for treatment of chronic anal fissure.

PATIENTS AND METHODS: In a quasi-experimental trial in a university hospital in Kerman, 50 patients diagnosed with chronic anal fissure received 20 units botulinum toxin ($n=25$) or underwent lateral internal sphincterotomy ($n=25$). All patients were evaluated for pain, bleeding and healing of the fissure from one to six months later by another surgeon. The data was analyzed by SPSS software with the Mann-Whitney and Fisher's exact tests.

RESULTS: One month after treatment, the rate of healing and bleeding in the operation group was better than in the toxin group ($P<0.05$), while pain was equal. After two months, none of the patients in either group had complications. After six months follow-up, bleeding, pain and healing were better in the operation group.

CONCLUSION: In the clinical evaluation, botulinum toxin is an effective alternative nonsurgical modality for the treatment of chronic anal fissure. We recommend botulinum toxin as the first step in treatment because of the 60% chance of cure with an easily performed treatment.

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Anal fissure, a split in the skin of the distal anal canal, is a common problem that causes substantial morbidity in people who are otherwise healthy. Anal fissure is characterized by pain on defecation, rectal bleeding and spasm of the internal anal sphincter. Spasm of the internal anal sphincter plays a central role in the pathogenesis of the disease.^{1,2} Patients typically have a high resting anal sphincter pressure and infrequent spontaneous relaxation of the internal anal sphincter.³ Surgical sphincterotomy, which provides symptomatic relief and healing, is highly effective but can be associated with permanent complications.^{1,4} Alternative medical and noninvasive approaches have been proposed to treat this condition without any risk of permanent internal sphincter injury. One of these methods is chemical denervation with botulinum toxin,^{5,6} which may reduce anal pressure for three months or more, allowing the fissure to heal and eliminating the need for surgery. In this study, we compared injection of botulinum toxin with surgical sphincterotomy in the treatment of chronic anal fissure.

Patients and Methods

This study was a quasi-experimental trial. Consecutive adults with symptomatic chronic anal fissure were enrolled in the study. The diagnosis was based on the following clinical criteria: evidence of circumscribed ulcer, with a large sentinel tag of skin, indurations at the edges, and exposure of the horizontal fibers of the internal anal sphincter and symptoms (post-defecatory or nocturnal pain, bleeding, or both) lasting for more than 2 months. Patients with acute fissure, or fissure associated with other conditions (i.e., inflammatory bowel diseases, HIV infection, hemorrhoids, fistula in ano, anal abscesses, anal or perianal cancer) and those who had undergone previous surgical procedures in the anal canal were excluded.

After giving informed consent, eligible patients underwent treatment with either botulinum toxin A or lateral internal anal sphincterotomy, depending on which procedure

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the patient preferred. Surgeons evaluating the results were blinded to the procedure. Botulinum toxin A (*Botox, Allergan, Irvin, UK*) was diluted in saline and each patient received botulinum toxin (for a total 20 unit) administered as two injections for an equal volume on each side of the anterior midline of the internal anal sphincter. No sedation or local anesthesia was used during the procedure.

The end point of the study was complete healing after treatment. The treatment was considered successful if the fissure healed. Persistence of the fissure in the absence of symptoms was considered as symptomatic improvement. Monthly for 2 months and at 6 months after treatment, another surgeon in the outpatient department examined all patients and recorded healing, bleeding, and pain.

Statistical analysis was conducted with SPSS, version 10 for Windows. The results are expressed as ordinal data; differences between two groups in sign and symptom rates were compared with the Mann-Whitney test and differences in percentages were analyzed with the Fisher's exact test. All P values are two tailed. A P value of less than 0.05 was considered statistically significant.

Results

Twenty-five patients were randomly assigned to receive injection of botulinum toxin, and 25 were assigned to surgical sphincterotomy. All patients reported severe pain after defecation and each had a posterior anal fissure with a large sentinel tag of skin and exposed internal anal sphincter fibers. The groups were matched with regard to age, sex, duration of symptoms and occupation (Table 1).

One month after treatment, 16 patients in the toxin group and all patients in the operation group had a healed fissure ($P<0.01$). The rate of pain relief in the toxin group was equal to the operation group, while bleeding was significantly higher in the toxin group ($P=0.02$) (Table 2). At the two-month evaluation, the rate of healing and symptoms were the same as in the previous month. Five patients in the toxin group had symptomatic improvement after 2 months. They had persistent fissure without any symptoms. Comparing complications between groups, gas incontinency was significantly more frequent in the operation group after one month (2/11; $P<0.01$), but pain was more frequent in the toxin group (0/5; $P<0.05$). After two months of follow up none of the patients in either group had complications.

At the third follow-up evaluation 6 months later, 5 patients in toxin group and 2 patients in the operation

Table 1. Baseline characteristics of 50 patients with chronic posterior anal fissure.

	Toxin group (n=25)	Operation group (n=25)
Male/Female	1/24	5/20
Age (years) (mean±SD)	35.5±9.3	33±9.6
Duration of symptom (mean±SD)	18.2±24.7	10.1±8.5
Duration of Constipation (mo) (mean±SD)	9.3±9.6	8.5±6.7

Table 2. Symptoms in the two groups 1 month after treatment.

	Toxin group (n=25)	Operation group (n=25)
Bleeding (P=0.02)	No	16
	Yes	9
Pain (P=0.05)	No	23
	Yes	2

group had bleeding and 6 patients in the toxin group and one in the operation group had a little pain (Table 3). Healing occurred in all patients in the operation group and in 22 patients in the toxin group ($P<0.05$). The recurrence rate after 6 months was 20% in the toxin group and 7% in the operation group.

Discussion

Botulinum toxin exerts its effects on the peripheral nerve ending at the neuromuscular junction, resulting in a flaccid paralysis due to irreversible and selective multiphasic blockade of acetylcholine.⁷ The toxin inhibits contraction of gastrointestinal smooth muscle. Therefore, the toxin is effective in treating anal fissure when injected into internal anal sphincter, avoiding permanent complications. Chemical denervation with botulinum toxin has been proposed as a noninvasive alternative treatment for chronic anal fissure.^{5,6} Surgery for treating this condition is associated with a number of complications, most of which are minimized by judicious of surgical techniques.⁸

Our study demonstrates that botulinum toxin can be used in the outpatient department to treat chronic fissures. Maria and coworkers determined that botulinum toxin is more effective than placebo for treating anal fissure,⁶ with a healing score rate of 73.3%, approximately the same as our study (64%).

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Table 3. Symptoms in the two groups 6 months after treatment.

	Toxin group (n=25)	Operation group (n=25)
Bleeding (P=0.02)	No	20
	Yes	5
Pain (P<0.05)	No	19
	Yes	6
Healing (P<0.05)	No	3
	Yes	22

In our study, sphincterotomy was more effective than botulinum toxin. Previous studies have demonstrated a healing rate ranging from 60 to 70 percent,^{5,6} after a single injection of 15 or 20 IU of toxin in the internal anal sphincter. Our results are in this range. Most of our patients refused the second injection though in some studies a second injection has led to a higher success rate.

In one trial, a higher dose of toxin was more effective than the lower dose with respect to long-term healing and was not associated with a higher rate of complications.⁹ The choice of injection site could ameliorate the clinical outcome and can result in a greater decrease in resting anal pressure. In another trial, injection of botulinum toxin on each side of the anterior midline of the anus to the internal sphincter was more effective and had a higher success rate than posterior midline injection.¹⁰ A higher dose had a higher success rate without any increase of complications or side effects. Measurement of anal sphincter pressure is important in the evaluation of treatment for anal fissure.

The long-term history of chronic anal fissure after healing by means of this new nonsurgical modality is not well documented. Few studies have assessed long-term recurrence, and their follow-up periods

are short and heterogeneous. With 6 to 24 months of follow up, the recurrence rate varied from 0 to 8 percent.^{6,9,11,12} However, Minguez and co-workers, in a long-term follow up (42 months) after treatment of chronic anal fissure with botulinum toxin, showed a recurrence rate of 41.5%, which is quite different from those mentioned previously.¹² In our study the recurrence rate after 6 months was 20% in the toxin group and 7% in the operation group, which is a higher recurrence rate than other studies on toxin treatment.

In another study comparing these two methods with a longer follow up than in our study they had better results and at 12 months the success rate was 75.4 percent in the botulinum group while the complication rate was higher in sphincterotomy group.¹³ Though the success rate in the toxin group was less than in the surgical group, it was performed without hospital admission, without anesthesia or incision and without complicated postoperative care. When we offer this type of therapy to patients all were eager to receive it despite its experimental nature.

Because spasm of the anal sphincter has been noted in association with anal fissure, for many years the aim of treatment was to reduce hypertonia of the sphincter. We have been unable to perform anal manometry because it is not available in our department. However, in the clinical evaluation it seems that botulinum toxin is an effective alternative modality for treatment of chronic anal fissure. We recommend injection of botulinum toxin as the first step in treatment of chronic anal fissure because of the 60% chance of cure with an easily performed treatment. Different modalities of therapy, like topical nitroglycerine ointment,¹⁴ which have not been evaluated in the treatment of this condition in Iranian patients, should also be considered for treatment of anal fissure.

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