

ORIGINAL ARTICLE

BILATERAL VERSUS POSTERIOR INJECTION OF BOTULINUM TOXIN IN THE INTERNAL ANAL SPHINCTER FOR THE TREATMENT OF ACUTE ANAL FISSURE

By

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Aim: comparison of bilateral versus posterior injection of botulinum toxin in the internal anal sphincter for treatment of acute anal fissure and prevention of chronicity.

Methods: Forty patients with acute anal fissure were randomly divided into two equal groups. Group I patients were treated by injecting 20 units of Botulinum toxin on each lateral side of the internal anal sphincter. Group II patients were treated by injecting 25 units of Botulinum toxin in the midline posteriorly.

Results: Mean period for complete pain relief was 8.45 ± 7.41 days in group I and 7.20 ± 7.19 days in group II. Mean time of healing was 5.20 ± 1.85 weeks in group I and 5.40 ± 2.01 weeks in group II. Two patients (10%) in group I and 3 patients (15%) in group II showed partial healing. Fissure recurred to 4 patients (20%) in group I and 3 patients (15%) in group II.

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

Keywords: Chemical sphincterotomy, prevention of chronicity, anal pain.

INTRODUCTION

Anal fissure is a common, painful condition that causes significant morbidity mostly in young adults. It is a split in the skin of the distal anal canal. The classic symptoms are intense pain on or after defecation and anal bleeding.⁽¹⁾ Anal fissures are nearly always single, and they have predilection for the posterior midline location and less commonly for the anterior midline where one of ten fissures is located.⁽²⁾

Anal fissure is clinically differentiated into acute and chronic. The point at which an acute fissure becomes chronic is contentious, but published work suggests symptoms lasting for more than two months are undeniably chronic.⁽³⁾

Most anal fissures are caused by stretching of the anal mucosa beyond its capability. Many acute anal fissures will heal spontaneously or by medical treatment. Recurrence rates range from 30-70% if treatment is

abandoned after the fissure is healed.⁽⁴⁾ Some fissures become chronic and will not heal. The most common cause for this is spasm of the internal anal sphincter muscle. This spasm causes poor blood flow to the anal mucosa, hence producing an ulcer which does not heal since it is deprived of normal blood supply.⁽⁵⁾

Aggressive treatment of acute anal fissure with the recently named chemical sphincterotomy may prevent its evolution to chronicity.

Botulinum toxin causes denervation of the internal anal sphincter by preventing the release of acetylcholine from presynaptic nerve terminals. Paralysis occurs within few hours, but the transmission of neuromuscular impulses resumes after the growth of new axon terminals. Temporary weakness of the internal anal sphincter occurs for three to four months.^(6,7) Authors tried bilateral injection Botulinum toxin in the internal anal sphincter to treat chronic anal fissure.^(8,9)

The aim of this study is to evaluate the efficacy of injection of Botulinum toxin into the internal anal sphincter for treatment of acute anal fissure and prevention of chronicity and to compare two sites of Injection of Botulinum toxin; bilateral versus posterior.

PATIENTS AND METHODS

This study was performed in the General Surgery Department, Ghodran General Hospital, KSA during the period from October 2005 to February 2008 on 40 patients with acute posterior anal fissure randomly divided through computer randomization program (www.randomization.com) into two equal groups. Patients having other anal pathology (i.e., inflammatory bowel diseases, hemorrhoids, anal fistula or anal abscess) were excluded from this study. Full explanation of procedures and patient consent were assured before inclusion in the research. The study protocol was approved by the Ethics Committee of Ghodran General Hospital, KSA.

All patients were diagnosed as having acute anal fissure based on their medical history and physical examination. Pain was evaluated using pain visual analog scale⁽¹⁰⁾ before treatment. All patients were treated by the same surgeon on outpatient basis. Injection was formed in the left lateral position.

Group I patients were treated by injection of Botulinum toxin into the internal anal sphincter. The 100 units' vials of type A lyophilized Botulinum toxin (Botox, Allergan, Inc, Irvine, CA, USA) were diluted in saline to a concentration of 50 units per milliliter immediately before injection. With a 25-G needle, 20 units were injected on each side of the internal sphincter guided under direct vision and digital examination (a total of 40 units per patient). No sedation or local anesthesia was used during the procedure.

Group II patients were treated by a single injection of 25 units of Botulinum toxin with a 25-G needle into the internal sphincter in the midline posteriorly under direct vision and digital examination. No sedation or local anesthesia was used during the procedure.

Pain was evaluated using pain visual analog scale given to patient to do it at home daily. Healing was defined as complete re-epithelization of the fissure and absence of symptoms. Recurrence of fissure was defined by re-existence of fissure in anatomic exploration whether associated with symptoms or not.

All patients were followed up in visits at 2 weeks intervals for 8 weeks, then every month for 6 months. Telephone follow up was made every 2 months. Patients were advised to visit the hospital if they have any anal symptom. The mean length of follow up was 15.2±4.3

months. Patients were asked about the presence or absence of pain and bleeding on defecation. Patients were asked about the continence and about the appearance of any side effects. The anus was examined visually to assess healing of the fissure.

Statistical analysis: Quantitative variables were expressed as mean ± Standard deviation. Qualitative variables were expressed as frequency and percent. Quantitative parametric variables were compared between the two groups using unpaired student t-test, quantitative non-parametric variables were compared using Mann-Whitney test. Qualitative variables were compared using Chi-square test or Fisher exact test (when the criteria for using Chi-square were not sufficient). The power used was 0.80 while the level of significance was 5%.

RESULTS

Forty patients were included in our study, 23 females (57.5%) and 17 males (42.5%). Thirty seven patients (92.5%) were Saudi Arabian and 3 patients (7.5%) were of other nationalities. The age of patients ranged from 16 to 83 years with mean age of 36.85± 17.35 years.

Pain on defecation was the main presenting symptom in all patients (100% of patients). Constipation was present in 85% of patients. Bright red bleeding was less common presentations (65% of patients), while pruritus and mucous discharge were much less common (22.5% of patients). Table 1 summarizes some demographic data of patients.

Table 1. Clinical data of patients (Percentage to total).

	Group I	Group II	Total
Age range	16-79	19-83	16-83
Age mean	(34.37± 15.29)	(39.33± 18.65)	(36.85± 17.35)
Sex			
Females	12 (30%)	11 (27.5%)	23 (57.5%)
Males	8 (20%)	9 (22.5%)	17 (42.5%)
Presentation			
Pain	20 (50%)	20 (50%)	40 (100%)
Constipation	15 (37.5%)	19 (47.5%)	34 (85%)
Bleeding	11 (27.5%)	15 (37.5%)	26 (65%)
Pruritus	5 (12.5%)	4 (10%)	9 (22.5%)
Total	20 (50%)	20 (50%)	40 (100%)

Clinical results after management

Time of pain relief: In group I, 5 patients (25%) reported partial pain relief at the passage of the first motion. Mean period of complete pain relief was 8.45±7.41 days. In group II, 7 patients (35%) reported partial pain relief at the passage of the first motion. Mean period of complete pain relief was 7.20±7.19 days. The difference between the two groups regarding time of pain relief was not statistically significant Table 2.

Table 2. Period of complete pain relief.

Time of pain relief	Group I	Group II	P-Value
First motion	5 (25%)	7 (35%)	>0.05
Two weeks	12 (60%)	12 (60%)	>0.05
Three weeks	2 (10%)	0	>0.05
Four weeks	1 (5%)	1 (5%)	>0.05
Mean period of pain relief	8.45±7.41 days	7.20±7.19 days	>0.05

Time of complete healing: At the first follow up visit two weeks after Botulinum injection, complete healing was not recorded in any patient. After 4 weeks: 13 patients (65%) in group I and 12 patients (60%) in group II showed complete healing. After 6 weeks other 3 patients (15%) in each group showed complete healing. After 8 weeks 2 patients (10%) in each group showed complete healing but 2 patients (10%) in group I and 3 patients (15%) in group II showed still partial healing. Mean time of healing was 5.20 ± 1.85 weeks in group I and 5.40 ± 2.01 weeks in group II. The difference between the two groups regarding time of complete healing was not statistically significant Table 3.

Table 3. Time of complete healing.

Time of healing	Group I	Group II	P-Value
Two weeks	0	0	>0.05
Four weeks	13(65%)	12 (60%)	>0.05
Six weeks	3 (15%)	3 (15%)	>0.05
Eight weeks	2 (10%)	2 (10%)	>0.05
Partial healing	2(10%)	3 (15%)	>0.05
Mean Time of healing	5.20±1.85 weeks	5.40 ±2.01 weeks	>0.05

Complications: Hematoma after injection occurred in 2 patients (10%) of each group. Partial healing occurred in 2 patients (10%) in group I and 3 patients (15%) in group II. The difference between the two groups was not statistically significant.

Recurrence: Recurrence of fissure occurred in 4 patients (20%) in group I and 3 patients (15%) in group II; 2 patients (10%) in group I and 2 patients (10%) in group II within 6 months after injection, 1 patient (5%) in group I within 9 months after injection and 1 patient (5%) in each group within 12 months after injection. Second trial of Botulinum injection was good to achieve healing in 3 patients. The injection was done in the same location of the original injection. Other patients asked for operative treatment. They were referred to lateral internal sphincterotomy. The difference between the two groups was not statistically significant Table 4. Only one patient (2.5% of total number) of Group I did not complete 1

year follow up. Our hospital exists in a tribal area in KSA where patients are well adherent to their tribes. Mobile communications make it easier to contact patients.

Table 4. Time of Recurrence.

Time of Recurrence	Group I	Group II	P-Value
Three months	0	0	>0.05
Six months	2 (10%)	2 (10%)	>0.05
Nine months	1 (5%)	0	>0.05
Twelve months	1 (5%)	1 (5%)	>0.05
Total	4 (20%)	3 (15%)	>0.05

DISCUSSION

Acute anal fissure is a common painful condition. The cause is controversial. Current theories suggests it as an initial traumatic tear that fails to heal because of the internal anal sphincter spasm, generating high pressure into the anal canal and leading to secondary local ischemia of the anal mucosa.⁽¹¹⁾ Treatment aims at improving the blood supply to the ischemic area in order to facilitate healing by reducing the resting anal pressure of the internal anal sphincter. Traditional surgical techniques for treatment include anal dilation and partial division of the internal anal sphincter, which may be complicated by incontinence.⁽¹²⁾ This significant complication led to a search for alternative therapies for the treatment of anal fissure. The alternative options of chemical sphincterotomy include topical glyceryl trinitrate,⁽¹³⁾ diltiazem,⁽¹⁴⁾ Botulinum toxin,^(8,9,15) bethanechol,⁽¹⁴⁾ indoramin,⁽¹⁶⁾ and nifedipine.⁽¹⁷⁾

Botulinum toxin causes temporary weakness of the internal anal sphincter for three to four months.⁽¹⁸⁾ Studies of chronic anal fissure demonstrated a healing rate ranging from 60 to 76 percent after a single injection of 15 or 20 units of Botulinum toxin in the internal anal sphincter.⁽¹⁹⁾ Sajid et al.⁽²⁰⁾ recommended Botulinum toxin as a first-line therapy for chemical sphincterotomy in patients of chronic anal fissure. A study on patients treated with 15 or 20 U of 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 higher rate of complications.⁽²¹⁾

It is commonly believed that if acute anal fissure is aggressively treated, it can heal preventing the development of chronic fissure. In the present study Botulinum toxin injection caused evident pain relief at the passage of the first motion in 25% of group I patients and 35% of group II patients. Most patients had their pain relieved within 8 days. Complete healing of fissure occurred after 5.20 ± 1.85 weeks in group I and 5.40 ± 2.01 weeks in group II. Recurrence of fissure occurred in 20% of group I patients and 15% of group II patients. Second trial of Botulinum injection was good to achieve healing in 3 patients. Other patients asked for lateral

internal sphincterotomy. Trials on medical treatment recorded recurrence rates ranging from 30-70% if treatment is abandoned after the fissure is healed.⁽⁴⁾

Our preferred operation for anal fissure is open lateral internal sphincterotomy. This agrees with García-Granero et al,⁽²²⁾ who evaluated open and closed sphincterotomy. Closed sphincterotomy was associated with higher fissure persistence and recurrence rates than open sphincterotomy. Open sphincterotomy was significantly associated with a higher proportion of complete sphincterotomies than closed sphincterotomy. Complete sphincterotomy was associated with lower fissure persistence or recurrence rate but higher incontinence scores than following incomplete sphincterotomy.

There are no similar published studies, to our knowledge, for comparison. Katsinelos et al.⁽²³⁾ investigated the efficacy of topical application of 0.5% nifedipine ointment in healing acute anal fissure and preventing its progress to chronicity. Twenty-seven of 31 patients completed an 8 week treatment course, of them 85.2% achieved a complete remission indicated by resolution of symptoms and healing of fissure. Recurrence of symptoms occurred in 16% of these patients who were successfully treated with an additional 4 week course of 0.5% nifedipine ointment. They concluded that Topical 0.5% nifedipine ointment, used as a chemical sphincterotomy, appears to offer a significant healing rate for acute anal fissure and might prevent its evolution to chronicity.

A single injection posterior to the fissure was easier, less painful to patients and as effective in pain relief. It did not decrease the efficacy of treatment. Increasing the dose of the injection did not lead to any adverse effects. Total reduction of injected dose per patient was an advantage.

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

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