

# Botulinum Injection and Sphincterotomy for Management of Anal Fissure in Terms of Healing of Anal Fissure: A Randomized Controlled Trial

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## ABSTRACT

**Aim:** To compare the efficacy of botulinum injection with lateral internal sphincterotomy done for management of anal fissure in terms of healing of anal fissure

**Study design:** Randomized controlled trial

**Setting and duration:** Department of General Surgery, K.E. Medical University, Lahore from April, 2019 to Oct, 2019

**Methodology:** All 350 (175 cases in each group) cases meeting inclusion criteria were enrolled through department of Surgery KEMU. Patients were randomly allocated in two groups, group A and B by Lottery method. Patients in group 'A' received treatment with 0.5 ml (20 units) Botulinum toxin injection on each side of anal fissure in the internal anal sphincters under direct vision and digital examination at 3 or 9 o'clock position in lithotomy position under strict aseptic measures by single expert surgeon having at least five years' post fellowship experience. Patients in group 'B' underwent lateral internal anal sphincterotomy under general anesthesia by single expert surgeon also having at least five years' post fellowship experience. Patients were discharged on 1st post operation day on oral antibiotics, analgesics, stool softeners and were advised sitz bath. In both groups, patients were followed up for 2 months.

**Results:** The mean age of all patients was  $43.09 \pm 10.68$  years while the mean age in Group-A was  $43.17 \pm 10.32$  years and in Group-B was  $43.02 \pm 11.06$  years. The efficacy in Group-A was seen in 158 (90.3%) while the efficacy was seen in 114 (65.1%) of Group-B, the efficacy of treatment was higher in group-A when compared with Group-B, p-value < 0.001.

**Conclusion:** Botulinum toxin injection for the treatment of anal fissure has yielded higher rates of healing than lateral internal sphincterotomy. This suggests that botulinum injection could provide temporary relief from sphincter spasm, allowing for faster fissure healing and improved quality of life, with fewer risks of complications.

**Keywords:** Sphincterotomy, anal fissure, healing of anal fissure, rectal pain, anal pain, anal surgery

## INTRODUCTION

Anal Fissure (AF) is a disease of anal canal and is characterized by cracks or tears appearing on stratified squamous epithelium of anoderm<sup>1,2</sup>. The tear, being present in the squamous part of the epithelium, causes considerable pain, fresh bleeding during defecation. Anal fissures are a type of injury that occur in the anal area, and is estimated to affect 11% of people over their lifetime. It can lead to significant discomfort, missed days from work, and a reduced quality of life overall. Anal fissure occurs especially in young healthy adults without any other medical problems<sup>1</sup>.

Relieving pain caused by anal spasms can be accomplished through either surgical or chemical methods. The most common surgical treatment is lateral internal sphincterotomy which heals and relieves symptoms in over 90% of patients<sup>4</sup>. Although surgery is considered to be the most reliable and effective treatment for anal fissure, there are potential risks and side effects that require careful consideration before opting for the surgery<sup>5-7</sup>.

The risk of incontinence associated with surgical treatment for chronic anal fissures is very high, and so is the sphincter muscle hypertonicity and the ischemic nature of the fissures themselves. Despite this, researchers are still seeking an effective medical therapy or treatments that can help relax the sphincter<sup>4</sup>. When Botulinum toxin injection is given, the release of acetylcholine is suppressed which in turn leads to a decrease in resting anal pressure<sup>4</sup>.

A local study was conducted to evaluate the similar objective as of ours. The results showed that the most frequent complications were pain (68%), bleeding from the surgical site (25%) and sepsis (16%). Additionally, this technique also resulted in transient urinary retention in 9% of patients, as well as incontinence (8%) and recurrence of the fissure in 7% of them<sup>2</sup>.

The study discussed the use of botulinum toxin injections as a first line treatment for heal chronic anal fissures. It was found to be more effective than other treatments, with a healing rate of 86.2% reported within 10 weeks<sup>1</sup>.

We found only one local study that compared the effectiveness of Botulinum toxin injection and lateral internal sphincterotomy for treating anal fissures. It found that Botulinum toxin injection was more effective than lateral internal sphincterotomy in terms of healing, with an efficacy of 83.8% compared to 75.8% (p was less than 0.05)<sup>8</sup>.

Though data exists on local population separately on Botulinum toxin injection<sup>1</sup> and lateral internal sphincterotomy<sup>2</sup> and also only one study is available on their comparison. If we consider separate studies they favored their respective treatment while Botulinum toxin injection was preferred by Iqbal Z et al<sup>8</sup>.

They all have measured different outcome. So the current study is obligatory to compare both ways as side internal sphincterotomy is extensively used in our cases whose main concern remains its goods on anal continence. If in this study injection of botulinum toxin gives better results then, in future this reliable option can be used to provide temporary relief of sphincter spasm and allowing the fissure to heal early and to ameliorate patient's quality of life.

## MATERIAL AND METHOD

A total of 350 (175 in each group) were taken, the sample size is calculated using efficacy of Botulinum toxin injection as 86.2% and of lateral internal sphincterotomy as 75.8%<sup>8</sup> at 5% level of significance and 80% power of test. All patients both male and female 18-60 years of age suffering from anal fissure for more than six weeks were included. Known cases of intestinal tuberculosis (was detected by history and previous medical record), Inflammatory bowel diseases (detected by Colonoscopy and biopsy) and Anorectal carcinoma (by proctoscopy and biopsy)

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Pregnant women due to risk of complications were excluded. Patients on anticoagulant therapy due to risk of bleeding were excluded.

Patients were admitted after taking prior informed consent and permission of ethical committee. All 350(175 cases in each group) cases meeting inclusion criteria were enrolled through department of Surgery KEMU. Their demographic data, history and examination findings was recorded.

Patients were randomly allocated in two groups, group A and B by Lottery method. Patients in group 'A' received treatment with 0.5 ml (20 units) Botulinum toxin injection on each side of anal fissure in the internal anal sphincters under direct vision and digital examination at 3 or 9 o'clock position in lithotomy position under strict aseptic measures by single expert surgeon having at least five years experience. Patients were sent home after one hour with stool softeners. Patients in group 'B' underwent lateral internal sphincterotomy under general anesthesia by single expert surgeon also having at least five years' experience. The procedure performed in lithotomy position under strict aseptic measures. Patients were discharged on 1st post operation day on oral antibiotics, analgesics, stool softeners and were advised sitz bath. In both groups, patients were followed up for 2 months. At follow up, patients were examined for healing (yes or no). All data was accumulated by researcher himself.

All collected data was analyzed in SPSS version 20. For quantitative data like age and duration of disease was introduced in form of mean ± S.D. Frequency (percentages) was calculated for qualitative variables like gender and healing of anal fissure. To compare healing of anal fissure Chi square test was applied. To address effect modifiers data was stratified for age, gender, obesity (BMI >30) and duration of disease. Post stratified Chi-square test was applied taking p-value to ≤0.05 as significant.

**RESULTS**

The mean age of all patients was 43.09 ± 10.68 years details are shown in Table -1. The mean duration of disease of all cases was 6.87±3.84 months. The efficacy in group-A was seen in 158(90.3%) while the efficacy was seen in 114(65.1%) of group-B, the efficacy of treatment was higher in group-A when compared with group-B, p-value <0.001 (Table 3). When data was stratified for age, among 18-39 years old cases, the frequency of efficacy was statistically higher in group-A (90.4%) as compared to group-B (62.7%), p-value <0.001 while in 40-60 years old cases, the frequency of efficacy was also statistically higher in group-A (90.2%) as compared to group-B (66.1%), p-value < 0.001 (Table 4). Among male cases, the frequency of efficacy was higher in group-A (91.5%) as compared to group-B (68%), p-value < 0.001, while among female cases the frequency of efficacy was also statistically higher in group-A (88.9%) as compared to group-B (61.5%), p-value < 0.001 (Table 5). In patients who had duration of disease as 1-5.99 months, the frequency of efficacy was higher in group-A (94.5%) as compared to group-B (77.8%), p-value < 0.05, while in cases having disease duration as 6-13 months, the frequency of efficacy was statistically higher in group-A (87.3%) as compared to group-B (56.3%), p-value < 0.001 (Table 6). Among obese patients, the frequency of efficacy was statistically higher in group-A (87.5%) as compared to group-B (62.7%), p-value < 0.05 while in non-obese cases the frequency of efficacy was statistically higher in group-A (90.9%) as compared to group-B (65.6%), p-value < 0.001 (Table 7).

Table-1: Details of age and duration of disease in both study groups

Study Groups	Age (years)			
	Mean	S.D	Minimum	Maximum
A	43.17	10.32	18	60
B	43.02	11.06	20	60
Total	43.09	10.68	18	60

Table 2:

Study Groups	Age (years)			
	Mean	S.D	Minimum	Maximum
A	6.92	3.83	1	13
B	6.82	3.87	1	13
Total	6.87	3.84	1	13

Table-3: Comparison of Efficacy in both study groups

Efficacy	Groups		Total
	A	B	
Yes	158(90.3%)	114(65.1%)	272(77.7%)
No	17(9.7%)	61(34.9%)	78(22.3%)

Chi-square = 31.938 P-value = <0.001 (Highly Significant)

Table-4: Comparison of Efficacy in both study groups with respect to Age groups (years)

Age groups	Efficacy	Groups		Chi-square	p-value
		A	B		
18-39	Yes	47(90.4%)	32(62.7%)	11.006	0.001*
	No	5(9.6%)	19(37.3%)		
40-60	Yes	111(90.2%)	82(66.1%)	21.020	<0.001**
	No	12(9.8%)	42(33.9%)		

\*\*Highly Significant \*Significant

Table-5: Comparison of Efficacy in both study groups with respect to gender

Gender	Efficacy	Groups		Chi-square	p-value
		A	B		
Male	Yes	86(91.5%)	66(68%)	16.153	<0.001**
	No	8(8.5%)	31(32%)		
Female	Yes	72(88.9%)	48(61.5%)	16.057	<0.001**
	No	9(11.1%)	30(38.5%)		

\*\*Highly Significant

Table-6: Comparison of Efficacy in both study groups with respect to Duration of disease (months)

Duration of disease	Efficacy	Groups		Chi-square	p-value
		A	B		
1-5.99 (months)	Yes	69(94.5%)	56(77.8%)	8.546	0.003*
	No	4(5.5%)	16(22.2%)		
6-13 (months)	Yes	89(87.3%)	58(56.3%)	24.188	<0.001**
	No	13(12.7%)	45(43.7%)		

\*\*Highly Significant \*Significant

Table-7: Comparison of Efficacy in both study groups with respect to BMI

BMI	Efficacy	Groups		Chi-square	p-value
		A	B		
Obese	Yes	28(87.5%)	9(60%)	4.611	0.032*
	No	4(12.5%)	6(40%)		
Non-obese	Yes	130(90.9%)	105(65.6%)	27.734	<0.001**
	No	13(9.1%)	55(34.4%)		

\*\*Highly Significant \*Significant

**DISCUSSION**

An anal fissure is a rip in the skin that runs down the distal part of the anal canal. This type of tear typically affects young people and can happen to either a male or a female. It is often found at the posterior commissure of the anal canal, and researchers believe that a reduction in blood supply to this area is the root cause of the condition. Recent research has revealed that local ischemia may play a role in the development of chronic anal fissures. However, the precise underlying cause of an anal fissure is still unknown at this time<sup>9</sup>.

Chronic anal fissure (CAF) is a condition that can be caused by increased resting anal tone of the internal sphincter muscle. This increased pressure can result in local ischemia due to the compression of the anodermal arteries. For this reason, lateral internal sphincterotomy, developed by Eisenhammer, was formerly accepted as the gold standard surgical procedure for chronic anal fissure. However, more recently, there has been a tendency

toward less intrusive management such as chemical sphincterotomy due to the potential risk of postoperative problems connected with the operation, such as incontinence of gas or stool. This is because of the potential danger of incontinence of gas or stool after the surgery<sup>10</sup>.

Isosorbidedinitrate, glyceryl trinitrate, calcium antagonists, and muscarinic agonists are just some of the topical pharmacological treatments that have been utilized with varied degrees of success. Other medicines include muscarinic agonists.<sup>11</sup> However, the primary drawbacks of these treatments are their limited usefulness over the course of time, as well as the possibility of adverse effects. Botulinum toxin (BT) has only just recently been given the green light for use in the treatment of chronic anal fissure<sup>12</sup>. An injection of BT produces a short-term weakening of the muscle that makes up the internal sphincter, which ultimately leads to a reduction in anal tone. This is because the injection blocks the release of acetylcholine.

Although the use of Botulinum toxin (BT) injections for therapeutic purposes has become popular worldwide, there is still considerable debate over whether or not there is a definitive recommendation for the injection of BT and what are the intervals between subsequent injections or how many injections can be administered in a single session. Limited research is available regarding the impact of varying doses of BT on postoperative flatulence or fecal incontinence<sup>13</sup>.

Lateral internal sphincterotomy (LIS) has been generally recognized as an appropriate treatment approach for chronic anal fissures (CAF), demonstrating effectiveness in over 90% of cases.<sup>14</sup> The principal consequence of this surgical treatment is the potential risk of permanent incontinence with gas, mucus, or, in some cases, stool. This can occur in 8-30% of patients. To reduce the chance of damaging the continence mechanism, therapies have been developed to induce a reduction in anal sphincter pressure, facilitating the healing of the anal fissure without worsening the incontinence<sup>15</sup>.

The research found that a dose of 0.5ml (20 units) of Botulinum toxin injection yielded an efficacy of 83.8%, while a lateral internal sphincterotomy produced an efficacy of 75.8%, with a p-value lower than 0.05 suggesting that Botulinum toxin injection was significantly more effective<sup>8</sup>. In current study the efficacy in Group-A was seen in 158(90.3%) while the efficacy was seen in 114(65.1%) of Group-B, the efficacy of treatment was higher in group-A when compared with group-B, p-value < 0.001. We like above study also found Botulinum toxin injection as good choice of treatment.

A recent meta-analysis was performed to evaluate and compare the outcomes of botulinum toxin injection and lateral internal sphincterotomy for cases of chronic anal fissure. The analysis included a total of 489 participants from seven trials who fit the inclusion criteria. Results indicated that those undergoing lateral internal sphincterotomy had a higher healing rate and a lower incontinence rate than those on botulinum toxin injection, but with no major difference observed regarding complications between these two treatments. Additionally, the recurrence rate was significantly lower among those treated with lateral internal sphincterotomy. From the analysis, it appears that lateral internal sphincterotomy is the better option in terms of healing rate and preventing recurrences. That said, botox is considered safe and has a low risk of incontinence, making it a potential choice for some chronic anal fissure cases<sup>16</sup>.

Valizadeh et al conducted a similar trial. At the two-month visit, complete healing of the fissure was statistically more likely in the lateral internal sphincterotomy (LIS) group than in the botulinum toxin injection (BT) group (44% vs 88%, p=0.001). At the three-month visit, however, there was no significant difference in healing between the two groups. The BT group had a higher rate of fissure recurrence compared to the LIS group after six months (p<0.05). Additionally, the LIS group had a higher incidence of anal incontinence at the three-month follow-up, although the final percentage of incontinence was not significant (p>0.05).

Therefore, the study concluded that when treating chronic anal fissure, treatment should be individualized to account for varied patient needs and profiles. Botulinum toxin injection has a higher likelihood of recurrence, whereas LIS can provide rapid and permanent recovery, but with a higher risk of anal incontinence<sup>17</sup>. In 2010, a large prospective controlled randomized study assessed similar outcome Results showed that surgical sphincterotomy yielded a significantly higher healing rate (p = 0.0086; 95% CI = 7.38-45.69%), as well as a lower recurrence rate (p = 0.0111; 95% CI = 6.6846.13%), compared to the BT injection. However, the latter was linked to a lower risk of anal incontinence (p = 0.0338; 95% CI = -1.6427.53%) in comparison to LIS. Thus, the study concluded that LIS is the preferred treatment for uncomplicated chronic anal fissures due to its higher healing rate and lower recurrence rate, though BT injections can be used as a simple, noninvasive alternative that avoids the risk of incontinence<sup>18</sup>.

Another study compared the efficacy of injection of botulinum toxin and surgical sphincterotomy for the treatment of chronic anal fissure. After two months, it was found that none of the patients in either group had developed any complications. At six-month follow-up, the results from the operation group revealed significantly greater improvements in bleeding, pain and overall healing. As a result, it was concluded that botulinum toxin can be utilized as a non-surgical alternative for the treatment of chronic anal fissure, providing a 60% success rate from a quickly administered treatment<sup>19</sup>.

Similarly, another non-randomized study aimed to compare the effectiveness and reduction of anal sphincter pressures of lateral internal sphincterotomy and botulinum toxin injection as treatments for chronic anal fissure. Patients chose either procedure for their treatment. The results of the study had demonstrated that the maximum resting pressures decreased significantly among the participants of the surgery group (from 104±22mmHg to 86±15mmHg; p <0.05) and the botulinum toxin group (from 101±23 mmHg to 83±24mmHg; p<0.05). The botulinum toxin group experienced a more significant decrease from 117±62mmHg to 76±34mmHg (p <0.01). Moreover, the healing rate for the fissures was 70% in the botulinum group and 82 percent in the surgery group, with no significant difference between the two (p >0.05). The results suggest that both treatments are effective in decreasing the pressures and the healing rate of chronic anal fissure<sup>20</sup>.

A randomized, prospective study was conducted to compare the effectiveness of botulinum toxin injection to lateral internal anal sphincterotomy in the treatment of chronic anal fissure. The trial included 61 patients in the botulinum toxin group, who received an injection of 20-30 U of type A botulinum toxin into the internal anal sphincter. After two months of treatment, 45 of the 61 patients had experienced complete healing, and the remainder required an additional injection. At six months, the total healing rate reported for the botulinum group was 86.9%. For the 50 patients in the sphincterotomy group, the healing rate at two months was 98%, and after six months, the healing rate was 96.4%. Even though the healing rate in the sphincterotomy group was higher, the rate of complications was substantially higher with 8 reported incidents of incontinence compared to none in the botulinum group. Recovery time was much faster in the botulinum group, returning to daily activities within 1-14.8 days (mean 5.7 days) compared to the sphincterotomy group. The results of this trial suggest that, while botulinum toxin injection is an effective treatment for chronic anal fissure that is associated with fewer complications and a faster recovery time than sphincterotomy, it requires occasional repeat injections, and the healing process is slower<sup>21</sup>.

## CONCLUSION

Botulinum toxin injection for the treatment of anal fissure has yielded higher rates of healing than lateral internal sphincterotomy. This suggests that botulinum injection could provide temporary

relief from sphincter spasm, allowing for faster fissure healing and improved quality of life, with fewer risks of complications

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