



TREATING CHRONIC ANAL FISSURE: A NON-RANDOMIZED CONTROLLED TRIAL COMPARING BOTULINUM TOXIN INJECTION AND LATERAL INTERNAL SPHINCTEROTOMY

Dr. Umair Ahmed¹, Dr. Muhammad Zulqarnan^{2*}, Dr. Aisha Arshad³, Dr. Muhammad Hassan Azad⁴, Dr. Adil Dawach⁵, Dr. Daniyal Mehboob Panhwar⁶, Dr. Duaa Fatima⁷, Dr. Haadia Safdar⁸, Dr. Muhammad Shehbaz⁹

¹Assistant Professor of Surgery, Nishtar Medical University, Multan - Pakistan

^{2*}Post Graduate Resident Surgery, Bahawal Victoria Hospital Bahawalpur - Pakistan

³Consultant General Surgeon, District Provincial Hospital Quetta - Pakistan

⁴Post Graduate Surgery, Capital Hospital, CDA, Islamabad - Pakistan

⁵Registrar GS, Jinnah Postgraduate Medical Centre, Karachi - Pakistan

⁶Surgical Resident, Jinnah Postgraduate Medical Centre, Karachi - Pakistan

⁷Medical Officer, Jinnah Postgraduate Medical Centre, Karachi - Pakistan

⁸Clinical Trust Fellow – Urology, Medway NHS Foundation Trust - United Kingdom

⁹Medical Officer, Ali Akbar Surgi Med Hospital, Depalpur - Pakistan

***Corresponding Author:** Dr. Muhammad Zulqarnan

*Post Graduate Resident Surgery, Bahawal Victoria Hospital Bahawalpur - Pakistan
zqriaz25@gmail.com

Abstract

The administration of botulinum toxin through an injection within the sphincter muscle has emerged as a possible substitute for the traditional method of treating chronic anal fissure, which involves cutting the internal sphincter muscle on the side. This non-randomized study aimed to investigate the effects of botulinum toxin injection therapy and lateral internal sphincterotomy on reducing anal sphincter pressure in persons with chronic anal fissure. Anal manometry measurements were conducted prior to and two weeks following interventions, and individuals with the condition were had the option to choose between the two treatment techniques. Following the therapy, there was a significant decrease in the maximal resting pressures of both groups, and the magnitude of this impact was similar. The botulinum toxin group successfully decreased sphincter pressures, as evidenced by a substantial decrease in maximal squeeze forces. The healing rates for fissures were comparable between the groups treated with botulinum toxin and those who underwent surgery, with rates of 70% and 82% respectively. Throughout the 14-month observation period, there were no instances of recurring cracks. Botulinum toxin injection and lateral internal sphincterotomy demonstrated comparable efficacy in the treatment of chronic anal fissure, suggesting that both approaches are viable alternatives.

Keywords: Botulinum toxic, Efficacy, Tolerance, Anal treatment

Introduction

Patients suffering from chronic anal fissures (CAF) frequently report high resting anal pressure, which is an important component of the pathophysiology caused by the condition. Therapeutic

techniques that aim to reduce the pressures exerted by the anal sphincter have been applied in order to facilitate the healing of fissures (Jonas, 2001). This has been done in order to address the issue at hand. Because it requires either general or local anesthesia, lateral internal sphincterotomy (LIS), which is the most commonly used treatment for CAF and has a success rate of over 90 percent, is a significant disadvantage (Abcarian, 1982). However, it is the treatment that is utilized the most frequently. There is a potential that this surgical operation can result in long-lasting gas, mucus, or occasional inability to control bowel movements. This condition can affect anywhere from 8 to 30 percent of patients and may lead to complications such as the formation of abscesses and alterations in the shape of the anus (Pernikoff et al., 1994).

When treating simple chronic anal fissure (CAF), the intrasphincteric injection of botulinum toxin (BT) is believed to be a method that is reliable and effective (Oh et al., 1995). A comparison of this technique to a placebo has shown that it is more effective than the placebo. This strategy was adapted from the original research that Jost and Schmirgk (1993) conducted. Additionally, contrary to topical nitrate, which is another therapeutic option, BT has been shown to be more effective in treating the condition. Multiple studies have demonstrated that patients who received BT treatment did not suffer any long-term damage to their ability to maintain their continence (Maria et al., 1998). This is an extremely important finding. The primary objective of this research is to investigate and evaluate the efficacy of LIS and BT injection in the treatment of CAF at the same time. In addition to being prospective and controlled, the trial is not randomized. In addition, the purpose of the study is to investigate the impact that these methods have on the reduction of pressures in the anal sphincter, with the goal of gaining an understanding of the potential benefits and drawbacks associated with each approach.

Methodology

Recruitment of Patients

A cohort of adult participants who presented with symptomatic chronic anal fissures (CAF) was utilized in the research. The diagnosis of obstructive sleep apnea (CAF) was validated in accordance with particular criteria: the presence of a clearly delineated ulcer in the posterior region, a discernible skin tag, border hardening, and exposure of the horizontal fibers comprising the internal anal sphincter (IAS). In order to qualify for participation, individuals were required to have endured symptomatic signs for a minimum of two months, including but not limited to discomfort following defecation or at night, nighttime bleeding, or a combination of both. Complex fissures and significant secondary alterations, including scarring deformities, a prominent sentinel pile, and infiltration beneath the fissure, were excluded. Patients who consented to participate were given comprehensive information regarding the potential repercussions and concomitant negative effects of lateral internal sphincterotomy (LIS) and botulinum toxin (BT) injection. This measure guaranteed that the participants provided informed consent and had a complete understanding of the procedures.

Current Study Research Design

The therapy arms of the trial were designed based on patients' requests and were not randomized. Before starting the therapies, a comprehensive pre-treatment assessment was conducted on all subjects, which included a clinical examination of the fissure and anorectal manometry.

Procedure of Anal Manometry

Prior to commencing treatment and once more after 3 weeks, persons suffering with chronic anal fissures (CAF) underwent anal sphincter manometry. A pre-calibrated water perfusion system equipped with an octet of holes in the catheter, each positioned at a uniform distance of 0.5 cm, was employed for the manometry procedure. We employed software to store and analyze the data obtained from the manometry procedure. The reason for not performing an anal digital examination before to the manometry was to prevent any potential influence of anal dilatation on sphincter pressures. Before the study, all participants had intestinal preparation with an enema. Following the insertion of the

catheter into the rectum, patients were positioned in a comfortable left lateral posture, and their maximal resting pressure (MRP) and maximal squeezing pressure (MSP) were assessed. The MRP was obtained by averaging the maximum pressure readings from all holes using a stationary pull-through technique. The mean squeezing pressure (MSP) was obtained by subtracting the mean pressures created by voluntary squeezing for 5 seconds from the resting pressures, when all holes were situated inside the anal canal. To accurately measure sphincter pressures and prevent pressure interference, patients were instructed to contract their anus fully throughout the whole MSP test, while refraining from activating their abdominal and buttock muscles.

Operating and cutting into the lateral internal anal sphincter

The patient underwent either a spinal or general anesthesia while in the lithotomy posture during a lateral internal sphincterotomy (LIS) procedure. The skin encircling the anal border underwent a transverse incision as part of the procedure. The anoderm and intersphincteric groove were dissected before the sphincter was divided in direct view. Whether interrupted or open sutures were used to seal the wound depended on the method used.

Injection of Botulinum

The botulinum toxin was diluted with saline to produce a concentration of 40 U/ml. Both sides of the fissure were administered a dosage of 10 units of the diluted toxin injection, resulting in a combined total of twenty units in a volume of half a milliliter. The administration of this injection involved the use of a specialized insulin syringe equipped with a brief and slender needle measuring 10 mm in length, 26 gauge in thickness, and with a capacity of 1 mL. Patients were instructed to practice sitz baths and use anal tampons to aid in their recovery after the injection, especially during the initial weeks. The study aimed to track the occurrence of post-treatment problems experienced by patients and evaluate the extent of healing for chronic anal fissures (CAF). If the fissure underwent complete healing and subsequently formed a scar within a span of two months after the procedure, the treatment was considered to be successful.

Any failure to repair cracks was considered a treatment failure and was not included in the subsequent follow-up. The monitored complications encompassed the development of abscesses, thrombosed hemorrhoids, and incontinence, which involved issues such as soiling, flatus, and excrement. The secondary aim was to inhibit the recurrence of fissures, and patients whose fissures had healed were clinically observed for at least one year. Patients underwent reassessment at 6 and 12 months during the follow-up phase to see if there was a recurrence of the fissure. This entailed scrutinizing the area and reevaluating the patient's grievances.

Statistical Analysis

The findings are displayed as the mean value with the addition or subtraction of the standard deviation. The Student t-test and Mann-Whitney test were employed to compare manometric data groups, based on variations in standard deviations. We employed Fisher's exact test to examine the disparities in percentages. Statistically significant was defined as probabilities below 0.05.

Result

Table 1 the comparative clinical features of the two groups (N=21)

Patients Information	lateral internal anal sphincter (n=11)	Injection of Botulinum (n=10)
Gender	5/6	8/7
Age of Patient	45±15	40±20
Duration of Symptoms	8±3	7±5
Resting Pressure	101±19	105±21
Squeeze Pressure	110±50	99±47

Table 1 presents a comprehensive overview of the clinical features that were compared between the two groups, consisting of a total of 21 patients. The initial group consisted of eleven individuals who had lateral internal anal sphincterotomy (LIS), while the second group comprised ten patients who received botulinum toxin injections. The LIS group consisted of five males and six females, whereas the Botulinum injection group had eight males and seven females. The mean age of persons who had botulinum injections was 40 years old with a standard deviation of 20. On the other hand, those who received LIS had an average age of 45 years old with a standard deviation of 15. The LIS group experienced ongoing difficulties at 8 ± 3 months, whereas the Botulinum injection group continued to have symptoms at 7 ± 5 months. Furthermore, it is worth noting that both the LIS and Botulinum injection groups exhibited maximum resting pressures of 101 ± 19 and 105 ± 21 , respectively. The peak squeeze pressure in the LIS group was recorded as 110 ± 50 , while in the Botulinum injection group it was measured as 99 ± 47 .

Table 2 Treat comparison of pre and post anal pressure

Resting Pressure				Squeeze Pressure		
Group	Pre	Post	sig	Pre	Post	sig
BT	103 ± 25	75 ± 23	0.032	120 ± 71	78 ± 31	0.05
LS	105 ± 26	76 ± 25	0.021	80 ± 30	67 ± 27	0.001

The resting and squeeze pressures of both the botulinum toxin (BT) and lateral sphincterotomy (LS) groups were assessed before and after the procedure. The findings are presented and compared in Table 2. The baseline blood pressure (BP) in the BT group significantly decreased from 103 ± 25 mmHg before therapy to 75 ± 23 mmHg after treatment ($p = 0.032$). Similarly, the BT group's initial squeezing pressure was 120 ± 71 , and following therapy, it decreased to 78 ± 31 ($p = 0.05$). Following treatment, the LS group exhibited a significantly reduced resting pressure of 76 ± 25 , compared to the pre-treatment value of 105 ± 26 ($p = 0.021$). Following the therapy, the LS group experienced a significant decrease in pre-treatment squeezing pressure, dropping from an average of 80 ± 30 to 67 ± 27 ($p = 0.001$). The treatment groups exhibited a notable decrease in both resting and squeeze pressures, indicating the impact of BT injection and lateral sphincterotomy on anal pressures.

Discussion

This study affirms that botulinum toxin (BT) injection and lateral internal sphincterotomy (LIS) produce comparable outcomes in terms of internal anal sphincter pressures and rates of fissure repair. No instances of recurrence were observed throughout the long-term follow-up period. The study's findings indicate that patients suffering from chronic anal fissures (CAF) can be successfully treated using either LIS or BT injection therapies.

The presence of chronic anal fissures leads to a reduction in blood flow in the posterior anal region and an elevation in resting anal pressure that exceeds 30 mm Hg when compared to individuals without fissures (Chen et al., 1999). This is the foundation for the investigation. Ischemic damage may arise when there is a sustained increase in blood pressure, leading to a reduction in blood supply to both the sphincter muscle and the overlying epithelium. Consequently, therapies targeting the reduction of pressure on the internal anal sphincter (IAS) have been employed to expedite the healing process of fissures (Maria et al., 2000). The healing and recurrence rates of fissures vary significantly, even with the effectiveness of surgical procedures such as lateral sphincterotomy. The paper highlights that the incidence of fissure healing is reduced following LIS (82%), potentially because to the more cautious approach taken during sphincterotomy to prevent anal incontinence. No difficulties were observed over the 14-month follow-up period.

In order to avoid causing permanent harm to the anal sphincter, the study examined the use of injecting botulinum toxin into the sphincter as an alternate treatment for chronic anal fissure. The study highlights that botulinum toxin induces a temporary reduction in anal sphincter tone, facilitating the healing process of the fissure (Brisinda et al., 2002). Despite the anticipated temporary decrease

in sphincter tone, which was supposed to result in higher recurrence rates during botulinum toxin therapy, the study and other research have demonstrated astonishingly low rates of recurrence. The study observed that patients experienced a decrease in their maximal squeezing pressure, a brief duration of discomfort, and positive outcomes specifically for fissures located in the back after receiving botulinum toxin treatment.

Theoretically, the potential for anal incontinence after botulinum toxin treatment can be reduced as the toxin weakens the external anal sphincter (EAS) without completely inhibiting voluntary control, which is necessary to prevent incontinence. The study emphasizes the influence of the dosage and placement of botulinum toxin injections on the effectiveness of the treatment, primarily targeting the posterior region of the anal sphincter. Conversely, alternative studies propose that administering botulinum toxin in the front part of the body may have a greater impact on reducing the pressure of the sphincter when at rest.

Recent research comparing botulinum toxin with lateral sphincterotomy indicates that the latter treatment option offers a faster, more consistent, and longer-lasting healing effect, while the former treatment option appears to have a slower onset and loses its effectiveness over time with prolonged monitoring (Mentes et al., 2003). While the study acknowledges the possible advantages of lateral sphincterotomy, it also highlights the disadvantages, such as a greater likelihood of anal incontinence after surgery compared to the botulinum toxin group, which did not encounter any problems during the same period of observation. The study concludes that the way anal incontinence is seen as a complication of the treatment can impact the perceived advantage of lateral sphincterotomy.

Conclusion

Botulinum toxin (BT) injection is an excellent treatment for chronic anal fissures (CAF). The procedure's minimal invasiveness and seemingly negligible rate of complications distinguish it from surgical alternatives. It is important to note that BT injection treatment has the capacity to offer temporary periods of improvement. Additional, randomized controlled trials with extended follow-up periods are required to ascertain whether this therapeutic approach is superior to conventional approaches.

References

1. Jonas M, Scholefield JH: Anal Fissure. *Gastroenterol Clin North Am.* 2001, 30: 167-181.
2. Oh C, Divino CM, Steinhagen RM: Anal fissure: 20-year experience. *Dis Colon Rectum.* 1995, 38: 378-382.
3. Abcarian H, Lakshmanan S, Read DR, Roccaforte P: The role of internal sphincter in chronic anal fissure. *Dis Colon Rectum.* 1982, 25: 525-528.
4. Pernikoff BJ, Eisenstat TE, Rubin RJ, Oliver GC, Salvati EP: Reappraisal of partial lateral internal sphincterotomy. *Dis Colon Rectum.* 1994, 37: 1291-1295.
5. Lund JN, Scholefield JH: Aetiology and treatment of anal fissure. *Br J Surg.* 1996, 83: 1335-1344.
6. Jost WH, Schimrigk K: Use of botulinum toxin in anal fissure. *Dis Colon Rectum.* 1993, 36: 974-
7. Maria G, Cassetta E, Gui D, Brisinda G, Bentivoglio AR, Albanese A: A comparison of botulinum toxin and saline for the treatment of chronic anal fissure. *N Engl J Med.* 1998, 338: 217-220. 10.1056/NEJM199801223380402.
8. Brisinda G, Maria G, Bentivoglio AR, Cassetta E, Gui Albanese A: A comparison of injections of botulinum toxin and topical nitroglycerin ointment for the treatment of chronic anal fissure. *N Engl J Med.* 1999, 341: 65-69. 10.1056/NEJM199907083410201.

9. Chen R, Karp BI, Goldstein SR, Bara-Jimenez W, Yaseen Z, Hallett M: Effect of muscle activity immediately after botulinum toxin injection for writer's cramp. *Mov Disord.* 1999, 14: 307-312. 10.1002/1531-8257(199903)14:2<307::AID-MDS1016>3.0.CO;2-3.
10. Maria G, Brisinda G, Bentivoglio AR, Cassetta E, Gui D, Albanese A: Influence of botulinum toxin site of injections on healing rate in patients with chronic anal fissure. *Am J Surg.* 2000, 179: 46-50. 10.1016/S0002-9610(99)00255-X.
11. Brisinda G, Maria G, Sganga G, Bentivoglio AR, Albanese A, Castagneto M: Effectiveness of higher doses of botulinum toxin to induce healing in patients with chronic anal fissures. *Surgery.* 2002, 131: 179-184. 10.1067/msy.2002.119314.
12. Menteş BB, İrkörücü O, Akın M, Leventoğlu S, Tatlıcıoğlu E: Comparison of Botulinum toxin injection and lateral internal sphincterotomy for the treatment of chronic anal fissure. *Dis Colon Rectum.* 2003, 46: 232-237.
13. Brisinda G, Maria: Botulinum Toxin in the Treatment of Chronic Anal Fissure (letter). *Dis Colon Rectum.* 2003, 46: 1144-1147.