

ORIGINAL ARTICLE

Botulinum Toxin Injection Versus Lateral Internal Sphincterotomy for Chronic Anal Fissure: A Randomized Trial

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ABSTRACT

Objective: The objective of the study was to compare the outcome of botulinum toxin injection (BTI) and lateral internal sphincterotomy (LIS) for chronic anal fissure (CAF) in terms of efficacy and complications of both the procedures.

Patients and Methods: This prospective randomized trial was conducted in the Department of Surgery; Unit II Post-Graduate Medical Institution / Lahore General Hospital, Lahore over a period of one year. One hundred and thirty adult patients with CAF were randomized to have either Botulinum toxin injection (group A) or lateral internal sphincterotomy (group B). The outcome was measured in terms of pain relief, healing rate, recurrence of fissure and procedure related complications. Patients were followed up for 6 months.

Results: Majority of the patients were young with mean age of 39.35±13.24 years in group A and 35.31±12.19 years in group B. Posterior midline fissure was found in 86% and 92% of patients in group A and B respectively. At 6 months follow up, complete relief of pain was observed in 47 patients (72.3%) in group A and in 62 patients (95.4%) of group B (P= 0.0008). Healing rate was superior in surgical sphincterotomy group compared to chemical sphincterotomy group (P=0.0001). Moreover, there was no significant difference in the complication rate between the groups (P=0.6976).

Conclusions: Lateral internal sphincterotomy was more effective than the BTI in terms of pain relief and complete healing of CAF without any significant difference in the complication rate.

Key words: Chronic anal fissures, botulinum toxin injection, lateral internal sphincterotomy, incontinence, recurrence.

INTRODUCTION

Anal fissure is a painful linear tear in the distal anal canal, which extends from the anal verge proximally towards the dentate line, causing considerable pain and discomfort.¹ The etiology of chronic anal fissure (CAF) remains unclear. Trauma to anal mucosa due to excessive stretching during the passage of hard stool is believed to be the initiating factor in primary fissure. Then it causes the spasm of internal sphincter which leads to elevated resting anal pressure. Therefore the aim of the treatment is to reduce the tone of internal sphincter, which eventually improves the blood supply and allow the fissure to heal without compromising the continence of anal canal.^{2,3}

Lateral internal sphincterotomy (LIS) has been considered as a gold standard treatment for CAF with more than 90% success rate. However the main concern remains its effect on the anal

continence. The published incidence of incontinence to flatus and stool ranges from 0 to 34%.⁴⁻¹⁰ Hence, less invasive treatment options such as local application of calcium channel blocker (diltiazem), glyceryltrinitrate (GTN), and botulinum toxin injection (BTI) have been advocated and used with variable success.^{2,3,4}

Botulinum toxin injection was found to be more effective than other therapeutic options like nitrates and diltiazem with less severe adverse effects.^{11,12} It temporarily inhibits acetylcholine release into the synaptic gap, which eventually causes muscle relaxation and allows the fissure to heal without the fear of incontinence.¹³ The effectiveness of BTI in the healing of CAF has not been established well over the LIS. Therefore, the objective of this study was to compare the outcome of botulinum toxin injection and lateral internal sphincterotomy in patients with chronic anal fissure in terms of efficacy and complications of both the procedures.

PATIENTS AND METHODS

Between 1st January 2011 to 1st January 2012, this prospective randomized clinical trial was conducted in the department of surgery; Unit II, Post-Graduate Medical Institute at Lahore General Hospital, Lahore Pakistan. One hundred and thirty adult patients of either sex, with idiopathic CAF, who failed to respond conservative treatment of 6 weeks duration, were included in this study. They were randomized to receive either botulinum toxin injection (group A) or lateral internal sphincterotomy (group B) by using random number table.

Patients with previous perineal surgery, having secondary causes of anal fissure like tuberculosis, inflammatory bowel disease, anorectal carcinoma, sexually transmitted disease and acquired immune deficiency syndrome were excluded. In addition presence of associated anal conditions like anal stenosis, abscess, fistula and 3rd and 4th degree hemorrhoids or the patients on anticoagulation therapy were also excluded from the study. The study protocol was approved by local departmental research and ethical committee and informed consent was obtained from all the patients.

For group A patients, we used injection Neuronox (Medy-Tox Inc South Korea) for chemical sphincterotomy. Twenty units of Neuronox were injected at the lateral border of internal anal sphincter at 3 or 9'o clock position of each patient with insulin syringe of 25 gauge needle. After one hour of injection, patients were discharged home with follow up advice.

In group B, lateral internal sphincterotomy was performed under general or caudal anesthesia in lithotomy position. Inter-sphincteric groove was palpated. Vertical incision of about 1 cm was made at 3'o clock over the inter-sphincteric groove. The anal mucosa was separated from the internal sphincter all the way down to dentate line. The plains inside and outside the internal anal sphincter was dissected and sphincter was separated. The free lower edge of internal anal sphincter is then grasped and pulled drawn into the wound and its distal portion up to the upper edge of fissure was divided by scissor or electro-coagulation. Hemostasis was secured and the wound was left open. A loose pyodine soaked dressing was placed over the wound.

Patients were discharged on 1st post operative day after wound examination. Patients of both groups were instructed to have high fiber diet, oral analgesia, stool softener as required and regular

sitz bath. They were also advised to come for follow up visit on regular interval at 1st month, 3rd and 6th months to assess the postoperative pain relief, healing status of fissure and for any postoperative complication. The treatment was considered effective, if the patient became pain free and the fissure healed with a scar in 2 to 3 months time. Healing was defined as complete re-epithelization of fissure and absence of pain, while a failure was defined as non-epithelization of fissure and persistence of pain. Complications were described as incontinence, wound infection, hematoma and abscess formation.

The information regarding demography, clinical details, operative findings, post operative complications and follow-up were recorded on the proforma. The data analysis was done by using SPSS version 16.0. Mean of numerical or continuous variables were compared by student T-test. Categorical data comparison was made by Chi-Square test. The Probability value (P value) of less than 0.05 was considered as statistically significant.

RESULTS

One hundred and thirty patients of CAF, who fulfilled the selection criteria, were randomized in group A and B. The mean age of patients in group A and B was 39.35±13.24 and 35.31±12.19 years respectively. Overall male outnumbered the female (59.2% versus 40.8%). Posterior midline fissure was found in 86% and 92% of patients in group A and B respectively. Statistically there was no significant difference in the presence of skin tag with anal fissure between the groups. (Table No.1)

LIS was found more effective in the management of CAF than BTI. Forty three patients (66.2%) were pain free in group A, while 55 patients (84.6%) in group B had full relief of pain after one month of intervention (P=0.025). At 3 and 6 months follow up, there was a statistically significant difference of pain relief in both the groups (Table No.2). We observed rapid healing in group B compared to group A. After one month, 61.5% of the patients in group B while only 38.5% in group A had complete healing of their fissure (P=0.001). Similarly at 3 and 6 months follow up, there was statistically significant higher healing rate in LIS group than BTI group. However, there was no significant difference in the complication rates of both the groups. (Table No. 2).

In group A, we observed one case (1.5%) of hematoma formation after BTI, which was settled

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down on conservative measures. Two patients (3%) in group A had relapse of their symptoms and developed recurrence, but none of the patients in this group developed incontinence. On the other hand, 3 patients (4.6%) reported incontinence to flatus and loose stool, in group B which was

temporary and settled down within two to three weeks time. One patient (1.5%) in LIS group developed an abscess under the sphincterotomy incision site, which was managed by drainage.

Table 1: Characteristics of Patients

Number	Variables	Botulinum toxin Injection (Group A)	Lateral Internal sphincterotomy (Group B)	P-value
1	Number of patients	65	65	
2	Male to Female ratio (M:F)	1.32: 1	1.6: 1	
3	Mean Age (years)	39.35±13.24	35.31±12.19	0.073
4	Posterior Fissure	56 (86.2%)	60 (92.3%)	0.259
5	Presence of skin tag	24 (36.9%)	21 (32.3%)	0.580

Table 2: Outcome of interventions

Number	Outcome measures	Botulinum toxin Injection (Group A)	Lateral Internal sphincterotomy (Group B)	P-value
1	Relief of Pain at one month	43(66.2%)	55(84.6%)	0.025
2	Relief of Pain at 3 rd month	46(70.8%)	61(93.8%)	0.0013
3	Relief of Pain at 6 th Month	47(72.3%)	62(95.4%)	0.0008
4	Healing at one month	25 (38.5%)	40 (61.5%)	0.0141
5	Healing at 3 rd month	30 (46.2%)	62 (95.4%)	0.0001
6	Healing 6 th month	31 (47.7%)	63 (96.9%)	0.0001
7	Complications	3(4.6%)	4(6.15%)	0.6976

DISCUSSION

Anal fissure is a common anal pathology which is responsible for substantial impairment of the quality of life of otherwise healthy patients because of painful defecation and bleeding.¹⁴ It affects all age groups but common in young people that might be because of dietary habits of youth which leads to constipation. The mean age of 39 and 35 years in both our groups also falls within the published range.^{8, 10, 15, 16} Male affected more than female in our study similar to that of Arroyo A⁸ and Tayyab M et al.¹⁶ However Valizadeh N et al¹⁰ observed more female patients than male in their study. Primary CAF is located more often in the posterior midline than the anterior location, while the fissure secondary to other underlying conditions such as Crohn's disease, infectious diseases, trauma and malignancy may be found in other locations.² Almost 90% of the patients in our study had posterior fissure which is in accordance with the literature.^{4, 6, 16}

Anal fissure can be acute or chronic. Conservative management is the main stay of treatment of acute anal fissure, which includes analgesia, laxatives and topical application of anesthetics creams or jelly. However, when these conservative measures fail and the fissure stays for longer than 6 weeks, then it is labeled as chronic anal fissure which can be distinguished by the presence of longitudinal ulcer in anal canal, with indurated edges, exposed horizontal fibers of internal anal sphincter and increased tone of sphincter. The management of CAF aims to reduce the spasm of internal anal sphincter for early healing either by chemical or surgical sphincterotomy.¹⁵

Many conservative and surgical treatments have been proposed and practiced, but the management of CAF is still controversial.¹⁷ Lateral internal sphincterotomy remains the gold standard treatment for this condition with a healing rate of more than 90% and low recurrence rate. However it is associated with risk of surgical complications,

mainly the fecal incontinence.¹⁸ We found a healing rate of more than 95% in LIS group without any relapse of symptoms, like other investigators. However, we encountered 3 patients (4.6%) of temporary incontinence after LIS which is within the reported range.⁴⁻¹⁰ These cases of mild degree of anal incontinence were managed by medical treatment and dietary modification. The incontinence rate in LIS can be reduced by careful dissection of internal sphincter and limiting the cutting depth of sphincter.

Different medical therapies have been evolved in the last two decades, like GTN 0.2%, Diltiazem 2% and BTI to replace the surgical intervention.³ These drugs reduce the spasm of internal sphincter and allow the fissure to heal like that of LIS, hence named as chemical sphincterotomy. The use of nitrates and diltiazem has been extensively studied with variable success rate.^{2, 3} In a systematic review of medical therapy, Nelson questioned the efficacy of both nitrates and diltiazem, because of significant headache in up to 50% of patients with poor patient's compliance.¹⁹ Recently BT has proved its superiority in terms of better healing rate and minimum side effects over the other two methods.^{11, 12}

A healing rate of 41 to 88% has been reported with the use of BTI, without any significant risk of anal incontinence.⁶⁻¹⁰ Seventy two percent of our patients after BTI were completely pain free but clinical evidence of complete healing was achieved in about 48% of the patients at 6 months follow up. Slow healing rate and a progressive relapse up to 40% has been reported in the long term follow up.^{8, 20} This could be explained by the reversible effect of toxin after 2 to 3 months. Some studies considered longer duration of disease over 12 months and presence of a sentinel pile as the clinical adverse factors for the recurrence.^{6, 8, 20} Therefore, surgical sphincterotomy is recommended as the preferred treatment in such patients. Others described that success of BTI was mainly related to the site of injection and the toxin dose.⁶

We used a minimum recommended dose of 20 units. However some colleagues advocated a dose of 50 units for better outcome without any significant rise of adverse effects.²¹ Addition of tropical nitrates and fissurectomy with BTI to improve the healing process has also been recommended by some studies^{22, 23} while Asim M et al²⁴ found no difference in the outcome of addition of tropical nitrates with BTI. Two patients

(3%) developed recurrence in our study after BTI. Both the patients showed improvement by simple conservative means and didn't require any further treatment. We didn't encounter any degree of anal incontinence in BTI group as reported in literature.^{2, 18, 25} We think BTI is a simple, minimally invasive and less expensive outpatient procedure, which could be considered as a preferred treatment option in a selected group of patients, who are at risk of developing surgical complications or who don't want the surgery for CAF. Further randomized clinical trials with long term follow up are required to draw the firm conclusions about the optimum treatment of CAF.

CONCLUSION

LIS was more effective than the BTI in terms of pain relief and complete healing of CAF without any significant difference in the complication rate. However BT is simple, minimally invasive and an effective treatment of CAF, that could be recommended as the first-line of treatment in patients who are at risk of developing surgical complications or who want to avoid surgery.

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