BOTULINUM TOXIN: FOR SAFE AND EFFECTIVE NON-SURGICAL TREATMENT IN ACUTE AND CHRONIC ANAL FISSURES

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ABSTRACT

BACKGROUND

Fissure in ano is a common painful anorectal condition with high recurrence rates. It is commonly seen due to sedentary lifestyle, which involves prolonged sitting posture, mental stress, low fiber diet and lack of physical activity which causes chronic constipation. Irrespective to whichever modality of existing therapies that are used, the recurrences are common. The traditional surgical option like lateral internal sphincterotomy, which has been into practice since long time carries risk of incontinence. It is a need of an hour to rely on a treatment modality which should be simple, safe, effective and reversible with no permanent sequelae. In this study chemical sphincterotomy using injection, Botulinum toxin gives an alternative modality and proved to be the most safe and reliable non-operative option for treating both acute and chronic fissure in ano.

AIM AND OBJECTIVE

This present study clinically assesses the role of injection Botulinum Toxin A in the management of acute and chronic anal fissure.

METHODS

A total of 50 patients including both acute and chronic fissure-in-ano were treated with injection Botulinum toxin as first line of management.

RESULT

All patients were found to get symptomatic relief with high rates of fissure healing eventually. The lack of complications and simplicity in its administration makes it a reliable alternative to the currently practiced therapies.

CONCLUSION

Botulinum toxin offers a simple outpatient procedure for fissure-in-ano, which is safe without any significant complications. It carries the potential of being used as a first line of management in acute and chronic fissure-in-ano.

KEYWORDS

Fissure-in-Ano, Chemical Sphincterotomy, Botulinum Toxin.

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INTRODUCTION

Anal Fissure is most commonest cause of painful anorectal condition that constitute 70% of General Surgery Outpatient Department patients. Though it is an ulcer at the anal verge, but it leads to severe pain and distress to the patients.^[1,2] Acute anal fissures progress to chronic if not treated properly.^[3] Chronic fissures are characterised by a sentinel tag, hypertrophic anal papillae, anal spasm and/or fibrosis of the inner sphincter muscle.

History reveals that it was first described by Recamier in 1829, who recommended stretching the anal sphincter to treat this condition.^[4] Anal fissure affects all age groups, particularly young adults.^[3] Ninety percent of all fissures occur posteriorly and 10 percent anteriorly. Less than one percent of patients have both anterior and posterior fissures.^[4]

Clinical features includes severe excruciating pain at anus during the act of defecation.^[5] Acute anal fissures are extremely painful during defecation; the pain is cramp-like and may persist for hours. With chronic anal fissures, the pain may be less intense during defecation, but increases subsequently. Perianal eczema is often associated with chronic anal fissures. Hyperhidrosis of the anal fold aggravates these symptoms.^[6]

Conservative line of management for acute fissures consist of WASH regimen, which includes warm sitz bath 2-3 times a days for 10 minutes, digital application of Analgesic ointment at site of fissure, stool softners and high fiber diet.^[7] Etiopathogenesis of fissure-in-ano is painful spasm of internal sphincter muscle.^[8] Pathophysiology explains that the anoderm is more adherent to the underlying tissue in the posterior midline. The sphincter fibers form Y-shaped decussation in the posterior midline that is anchored to the mucosa. Blood supply to the anoderm at the posterior midline is significantly lower.

The reduced blood supply to the lesion is indicated by the absence of granulation tissue at the base of the fissure and a very slow growth of the anoderm even when the traditional conservative treatment eases the trauma due to hard faeces.

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A well-formed anal fissure rests directly over the internal sphincter and the circular fibers of this sphincter are visible on the floor of the fissure on naked eye inspection. The internal sphincter undergoes a state of spasm due to irritation and hypertrophies. Therefore, the treatment of this condition is aimed to reduce the internal sphincter hypertonia.^[9]

In the surgical treatment, lateral internal sphincterotomy is the most frequently performed surgical procedure for treatment of chronic anal fissure, which results in healing rate of 90% to 95%.^[4] It works by reducing the sphincter hypertonia, which is the main etiological factor in the development of chronic anal fissure.^[7] It may cause minor but permanent incontinence later.^[10] Minimally invasive other therapeutic alternatives were proposed to reduce anal pressure leaving the sphincter ring intact to avoid incontinence.^[6,7] Botulinum Toxin (BTX) injection in the internal sphincter muscle has become an acceptable alternative for internal anal sphincterotomy.^[11-12]

Botulinum toxin A (BTX A) is produced by Clostridium botulinum. Its action on hyperactive smooth muscles such as the anal sphincter is mediated by its action on the autonomic nervous system as in striated muscles. Sphincter manometry after BTX injection has demonstrated a lowering of resting intranal pressure.^[13]

It eliminates the spasm of the internal anal sphincter by blockage of neurotransmission without internal anal sphincter muscle disruption.^[13,14] Muscle paralysis occurs within hours and the effect remains for 3–4 months. This prolonged effect allows the fissure to heal. This effect is reversible because it is followed by axonal regeneration and formation of new nerve endings, which avoids the risk of permanent injury to the sphincter.^[15] BTX has a direct analgesic effect causing relief before the healing of the fissure.^[16] BTX has also a good safety profile and tolerability.^[17,18]

The lethal dose of BTX is dosage upto 3000 U for a 70-kg male.^[15] In majority of cases, total dose of 20U was sufficient to produce healing of the chronic anal fissure in our study. We aimed in this study to evaluate the effectiveness of BTX injection in the treatment of anal fissure.

MATERIALS AND METHODS

All patients presenting with painful defecation or painful bleeding per rectum were assessed in surgery outpatient department. Patients with single either anterior or posterior and both anterior and posterior combined fissures included both acute onset and chronic fissures were also included in the study.

Chronicity of fissure was confirmed by duration of symptoms, which was more than six weeks, typical circumscribed split, induration of edges and exposure of internal sphincter fibers with fibrosis of base. Multiple fissures secondary to local, inflammatory bowel or venereal pathology as well as those with previous surgical interventions were excluded.

A questionnaire of history and patient record including telephonic contact numbers were maintained. The clinical details were noted, which included inspection of perianal region, digital rectal examination and anoscopy.

No special investigations or anal manometry were undertaken.

Injections were administered in the outpatient office after verbal and written informed consent. The drug was injected in the left lateral position.

Dosage of injection Botox is 0.4 unit/kg body weight.

Botulinum Toxin type A of 100 unit vial was diluted with 10ml saline to a concentration of 10 units per ml. Therefore, each 1ml of insulin syringe loads 10 units of Botox. The anal region was then cleaned with betadine solution and spirit. After draping the part, the sulcus between the internal and external sphincters were palpated and each 5 units were injected into intersphincteric space in all the four quadrants, anterior, posterior, left and right side of the anal verge (Figure No. 1). So, totally 20 units of injection Botulinum Toxin were injected all together in a single patient. All patients tolerated the injection pricks uneventfully.

Patients were immediately discharged and allowed to home.

Close followup was advised at one, three and six weeks initially, thereafter at three and six months' duration.

Showing sites of Botox injections in all four quadrants in intersphincteric spaces

Fig. 1: Inj Botox given Intersphincteric space in 4 quadrants of perianal area

Summarisation of the above methods

Inclusion Criteria

1. Single anterior or single posterior fissure-in-ano.
2. Combined anterior and posterior fissure-in-ano.
3. Uncomplicated chronic fissure-in-ano with more than 6 weeks' duration.
4. Acute onset fissure-in-ano where the patient cannot even sit comfortably on a chair.

Exclusion Criteria

1. Children below 14 years of age.
2. Multiple fissure due to local, inflammatory bowel or venereal pathology as well as those with previous surgical interventions.
3. Perianal skin infection.
4. Perianal sepsis.
5. Complicated chronic fissure-in-ano with anal papilloma or infected fissure or associated with co-existing haemorrhoids.

Materials Used

1. Inj Botulinum toxin 100 units vial (Figure No. 2).
2. Insulin Syringes (Figure No. 3 and 4).

Method of Preparing the Dosages

A 100 units of Inj Botox diluted with 10ml of normal saline. Single 1ml of insulin syringe will load 10 units of Inj Botox. Therefore, 0.1ml = 1unit of Inj Botox. (Depending upon the weight of the patient, 20 – 25 units of Inj Botox were given in an average weight individual weighing between 60–70kgs of body weight).

Fig. 2: Inj Botox Vial

Fig. 3: Shows calibration

Fig. 4: Shows set of two insulin syringes

RESULTS

A total of 50 patients were included in the study. There were 26 males and 24 females with an average age of 43.5 years (Table 1). Majority of the patients complain of painful defecation or burning sensation while passing morning stools. Very few patients had associated trickling of blood along with stools. Many were from younger age group and gave a leading cause of prolonged period in sitting posture.

Majority had significant relief of symptoms after the chemical sphincterotomy starting as early as 3rd day post injection. None of them had any significant pain during injection session. No post procedure complications were noted like itching or swelling at site of injection. There was progressive improvement in symptoms during follow up with 46 patients becoming asymptomatic with healed fissures at three months.

Age in Years	Mean age is 43.5 years (22years - 65years)
Gender - Male:Female	26:24
Duration in Months	Mean duration =13 months (2 months - 24 months)
Location - Anterior (12 O'clock) or Posterior (6 O'clock) Position	Post 37, Ant 5, Both 8
Dosage - Injection Botox IU	Average units of Botox used is 25 (20-30 units)

Table1: Patient and Clinical Profile

Duration	100% Pain Relief	Percentage of Fissure Healed
1 st Week	30% (15 patients)	Nil
3 rd Week	56% (28 patients)	40% (20 patients)
3 Months	74% (37 patients)	93% (46 patients)

Table 2: Symptomatic Relief with Healing of the Fissures

DISCUSSION

Fissure-in-ano is a common and recurring anorectal painful surgical condition. The painful ulcer is considered to be ischemic in origin with hypertonicity and spasm of the internal sphincter contributing significantly to the pathology.^[19] This onset of pain is due to passage of hard stools which cause a tear over the posterior anal verge with characteristic symptoms of pain during defecation and streaking of stools with blood. Fear of pain and avoidance of defecation act leads to a vicious cycle of constipation and recurring anal trauma. The purpose of surgical treatment has been aimed to reduce sphincter spasm by division of its fibers. Wide maximal anal dilatation results in uncontrolled disruption of the sphincter with risk of high incidence of incontinence should be abandoned. Though a simple and effective procedure with healing rates of 90%-95% its drawback is the risk of permanent alteration of continence.^[20]

With multiple non-operative treatment modalities now available, there is an emerging trend of avoiding breach to the anal anatomy.^[21] Chemical sphincterotomy using oral medications or local topical applications aims to relax the spasm till fissure healing is complete without risk of permanent sphincteric injury. Calcium channel blockers have shown overall poor results despite prolonged use. The use of 0.2% nitroglycerin ointment requires repeated applications over few weeks. It has common side effects of headache, local burning and development of tolerance. Treatment results are also average compared to surgical therapy.^[22] Botulinum toxin offers the advantage of a single injection treatment as an office procedure. The drug has an early onset of 48 hours and prolonged paralytic effect lasting for 3-4 months. Pain relief is evident within a few days and progressive relief is obtained till three months. Most fissures heal within 4-8 weeks.

Treatment with Botox is cost effective with the entire treatment will cost approximately Rs. 3400 (Three thousand and four hundred Indian rupees) to the patient, while a surgical sphincterotomy costs nearly five times more than this amount. With high rate of pain relief and healing of the fissure

at three months, only few patients will require repeat injections or surgical intervention.

Lysy et al.^[23] quote long term healing rates of 70% with conservative methods. This study indicates that Botox as an agent for chemical sphincterotomy offers high symptomatic relief and healing rates. There is no risk of incontinence or irreversible sphincter damage and the treatment may be safely repeated in event of a recurrence. No special instruments or precautions were used in these cases. In busy surgical practice with constraints of operation time, Injection Botox offers a useful and effective outpatient alternative to operative treatment.

A larger study group with a longer follow-up period is required to define the recurrence rates and long term results. The knowledge that Botulinum toxin injection is a safe and effective therapy for symptomatic anal fissures is not new and has been reported in several studies. Spasm of the internal anal sphincter has been noted in association with chronic fissures for many years and therefore the treatment logically focuses on reducing hypertonia of the internal sphincter. It has been observed that injections of Botulinum toxin into intersphincteric space are also effective for treating fissures. The mechanism is probably diffusion of the drug both into internal sphincter as well as external sphincter muscle fibers.

Different factors may influence the response to Botulinum toxin. These factors are fibrosis of the internal anal sphincter that is more prominent at the site of the fissure than other sites in the smooth muscle which reduce the compliance of the internal sphincter, limiting diffusion of the toxin. Secondly, the ischaemia in the base of the posterior fissure that destroys the myenteric nervous fibers which are located between the circular and longitudinal smooth muscle layers for the entire length of the internal anal sphincter.

CONCLUSION

Injection Botox is suitable for treatment of acute and chronic uncomplicated anal fissure associated with increased anal sphincter tone and not associated or complicated by other associated anal diseases like fistula in ano or hemorrhoids.

Injection Botox is a simple procedure, easy to learn and can be done in the outpatient clinic without the need for sedation or local anesthesia. It is cost effective and leads to healing of the fissure thus avoiding surgery with its potential risk of incontinence. It has no side effects.

SUMMARY

Injection Botulinum Toxin is a useful, cost effective and safe alternative in the management of both acute and chronic anal fissures. It can be considered as first line of management for acute and chronic uncomplicated anal fissures.

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