

Is Botulinum Toxin Injection an Effective Treatment Option for Management of Chronic Anal Fissure

Gupta S^{1*} and Kolli VS²

¹Glangwilli General Hospital, Carmarthen, UK

²University Hospital of Wales, Cardiff, UK

*Corresponding author: Sapna Gupta, Glangwilli General Hospital, Carmarthen, UK

Copyright: Sapna Gupta, This article is freely available under the Creative Commons Attribution License, allowing unrestricted use, distribution, and non-commercial building upon your work.

Citation: Sapna Gupta, Is Botulinum Toxin Injection an Effective Treatment Option for Management of Chronic Anal Fissure, Ann Surg Onco Treat, 2024; 1(2): 1-5.

Published Date: 25-08-2024 **Accepted Date:** 20-08-2024 **Received Date:** 08-08-2024

Keywords: Chronic anal fissure; Management; Botulinum toxin

Abstract

Chronic anal fissure (CAF) is a common disease of the anoderm treated by colorectal surgeons. Pharmacological treatment is considered first-line therapy. An alternative treatment modality is injection of botulinum toxin (BT). However, there is a lack of consensus on the administration of BT among colorectal surgeons for the treatment of CAF.

A standardised protocol has been used to write a best-evidence topic. The discussion focused on whether injection of BT is effective for chronic anal fissure. For an electronic search of the relevant literature, the databases MEDLINE, the Cochrane Library, Scopus, and the Web of Science were used.

We found 65 articles. Out of these, only eight studies were found to be appropriate to answer the question. The outcome assessed was healing of the ulcer. The best evidence shows that botulinum toxin is safe and effective in the treatment of chronic anal fissure and can be safely used as an alternative to surgery.

1. Introduction

Using a structured literature review approach, a mini-review was created that offers evidence-based solutions to common clinical concerns. This mini-review was created using the International Journal of Surgery's design [1]. The quality of the available data was insufficient to undertake a meaningful systematic review or meta-analysis, based on a previous assessment of the literature.

2. Clinical scenario

A 42-year-old female patient presented to the colorectal clinic with a history of chronic anal pain and constipation. Investigations confirmed a localised chronic anal fissure. She was previously treated with topical glycerol tri-nitrate with no benefit. The surgical team looking after the patient is debating whether botulinum toxin will be an effective treatment of choice for her based on the best evidence available.

3. Three-part question

Is [botulinum toxin] safe and effective [non-operative management] for patients with [chronic anal fissure]?

4. Search strategy

A. Embase 2012 to August 2022 using the OVID interface:

[botulinum toxin] AND [management] AND [chronic anal fissure] AND [non-operative] OR [conservative]

B. Medline using the PubMed interface:

[chronic anal fissure] AND [management] AND [botulinum toxin]

The results were limited to English articles and human studies.

5. Search outcome

There were 65 potentially relevant articles. After removing duplicate references and unrelated literature, fifteen papers remained for consideration. After reading all of these publications, eight were chosen as having the most convincing evidence to address the topic.

6. Result

Table

Author, date of publication, journal and country	Study type	Patient group	Outcomes Follow up	Key results	Additional comments
Soltany et al., 2020 Journal of Family Medicine and Primary Care Iran	Prospective case series Level V	Total number of patients- 106 All patients received botulinum toxin treatment	Primary End point- Healing rate of anal fissure Follow up- 8 weeks	Healing rate- 84.9% Healing rate was higher in females than males Mean healing time- 4.68 weeks	Prospective study Single centre Short follow up period
Akalin et al., 2021 The American Surgeon Turkey	Retrospective Cohort Study Level III	Total number of patients- 44 Group 1- Conventional method for Botulinum toxin (26) Group 2- Endoanal ultrasound (EUS) guided Botulinum toxin- (18)	Primary End point- Healing rate of anal fissure. Follow up- 3 months	Healing rate- Conventional group (Group 1)- 69.23% EAUS group(Group 2)- 81.82%	Retrospective study Single centre Small sample size Short follow up period
Amorim et al., 2017 Porto Biomedical Journal Portugal	Retrospective Cohort Study Level III	Total number of patients- 81 All patients received botulinum toxin treatment	Primary End point- Healing rate of anal fissure. Follow up- 8 weeks	Healing rate- 96.8% Non-responders- 23 (28.3%) Reinjection needed- 7 (8.6%) of which 4 needed subsequent surgical treatment.	Retrospective study Single centre Small sample size Short follow up period
Brisinda et al., 2022 International Journal of Colorectal Disease Italy	Retrospective Cohort Study Level III	Total number of patients- 1003 All patients received botulinum toxin treatment	Primary End point- Healing rate of anal fissure. Follow up- 2 months	Healing rate- 77.7% Non-responders- 39 (3.9%) Reinjection needed- 184 (18.3%)	Retrospective study Single centre Large sample size Short follow up period
Ravindran et al., 2017 Techniques in Coloproctology Australia	Retrospective case-control study Level IV	Total number of patients- 222 Group 1- Low dose botulinum toxin (20-40 IU)- 75 Group 2- High dose botulinum toxin- (80-100 IU)- 147	Primary End point- Healing rate of anal fissure. Follow up- 25 months	Healing rate- Group 1- 87% Group 2- 83% In group-1 13% patients and in group- 2 16% patients needed second injection	Retrospective study Single centre Large sample size Long follow up period

				treatment with botulinum toxin	
Gulcu et al., 2021 Acta Chirurgica Belgica Turkey	Retrospective Cohort Study Level III	Total number of patients- 132 All patients received botulinum toxin treatment	Primary End point- Healing rate of anal fissure. Follow up- 24 months	Healing rate- Complete response -79.5% (105) Partial response- 13% (17) Failure to respond- 3% (4) Recurrence- 4.5% (6) patients	Retrospective study Single centre Small sample size Long follow up period
Dat et al., 2015 ANZ Journal of Surgery Australia	Retrospective Cohort Study Level III	Total number of patients- 101 All patients received botulinum toxin treatment	Primary End point- Healing rate of anal fissure. Follow up- 22 months	Healing rate- Complete response – 67% Partial response- 36% Failure to respond- 13% Recurrence- 32% Reinjection needed- 18.8%	Retrospective study Single centre Small sample size Long follow up period
Barbeiro et al., 2017 United European Gastroenterology Journal Portugal	Retrospective Cohort Study Level III	Total number of patients- 88 All patients received botulinum toxin treatment	Primary End point- Healing rate of anal fissure. Follow up- 5 years	Healing rate- Complete response – 45.4% (40) Partial response- 10.2% (9) Failure to respond- 29.5% (26) Recurrence- 14.7% (13)	Retrospective study Single centre Small sample size Long follow up period

7. Discussion

An anal fissure is a tear in the anal canal that is mostly found in the distal part of the canal.[2] Pain lasting more than 6 weeks is considered chronic. [2] It usually occurs between age of 20 and 40 years, equally across men and women, with an 8–11% lifetime prevalence. [2-3]

Despite the known risk of significant morbidity, such as faecal incontinence, lateral internal sphincterotomy remains the gold standard treatment for chronic fissures [4-6]. Therefore, a search for less intrusive techniques has been continuing. Examples include topical nitrates and injections of botulinum toxin. But because nitrates are linked to headaches, they are not well tolerated [4,7]. Botulinum toxin (BT) has been considered a potential treatment for chronic anal fissure ever since it was first discovered in 1993 [8] However, there are still questions regarding the pharmacotherapy of anal fissure with botulinum toxin.

In our study, we explored the safety and efficacy of botulinum toxin (BT) as a treatment for chronic anal fissure. Studies included in our review are to help identify best evidence-based practice for patients with chronic anal fissure (CAF).

In a prospective case series by Soltany et al. [9], 106 patients had 30U of botulinum toxin treatment, demonstrating that the treatment of chronic anal fissures with botulinum toxin is safe, effective, and has a low complication rate. The healing rate was also higher in females, patients with shorter symptom durations, and individuals with one fissure. Akalin et al [10] compared endo-anal ultrasound (EAUS)-guided BT injection with the conventional method in treating CAFs. This study showed that the healing rate in the EAUS group was clinically higher than that in the conventional group. This was retrospective study with small sample size of 44 patients, hence they recommended prospective study with large sample size. Amorim et al [11] conducted a retrospective cohort study of 81 patients in Portugal. This study adds to the body of research showing that BT considerably reduces anal pain and is an effective and

safe treatment option for treating chronic anal fissure. Another study with a large sample size of 1003 patients, Brisinda et al [12], showed that botulinum toxin injection into the internal anal sphincter is a safe and effective alternative to surgery for individuals with chronic anal fissure.

Ravindran et al [13] evaluated the effects of high dosage BT (80-100 IU) to low dose BT (20-40 IU) and reported that high-dose BT improves fissure healing rates and reduces recurrence in patients with CAF, with comparable long-term incontinence to low-dose BT. Another study conducted by Gulcu et al [14] supported that high-dose (100 IU) injection of BT into the internal anal sphincter is an effective and safe alternative to partial lateral anal sphincterotomy for the treatment of CAF.

Dat et al [15] in their retrospective study with a long follow-up period of 22 months demonstrated that BT is an effective strategy for CAF. Low doses of BT (33 IU) can be given with good efficacy. According to Barbeiro et al [16] in their retrospective study with a 5-year follow-up, BT may be the first-line therapy for chronic and medically refractory anal fissure, and a surgical approach should be recommended only for patients in whom repeated BT injections fail, or for patient preference, demanding a more aggressive treatment.

In conclusion, the evidence available in the literature does support that botulinum toxin is an effective and safe treatment for chronic anal fissure. Both high and low-dose botulinum toxin can be safely used as an alternative to surgery to prevent surgery-related complications. However, most of the studies included in this review were retrospective single-center studies. This highlights the need for large prospective studies for the efficacy of botulinum toxin in chronic anal fissures.

8. Clinical Bottom Line

According to six retrospective cohort study, one retrospective case control study and one prospective case series botulinum toxin is safe and effective treatment for chronic anal fissure and can be used as an alternative to surgery with good healing rate.

9. Limitation of the Study

1. Small sample size in some studies
2. All 8 studies were single centre studies
3. Most studies were retrospective rather than prospective
4. Short follow up period in 4 out of 8 studies.

References

1. Gupta S, Alawad AA, Dacosta K, Mahmoud A, Mohammed T. Operative versus non-operative management for perforated peptic ulcer disease. *Annals of Medicine and Surgery*. 2022; 104643.
2. Mapel DW, Schum M, Von Worley A. The epidemiology and treatment of anal fissures in a population-based cohort. *BMC gastroenterology*. 2014; 14(1): 1-7.
3. Amorim H, Santoalha J, Cadilha R, Festas MJ, Barbosa P, Gomes A. Botulinum toxin improves pain in chronic anal fissure. *Porto Biomedical Journal*. 2017; 2(6): 273-6.
4. Sinha R, Kaiser AM. Efficacy of management algorithm for reducing need for sphincterotomy in chronic anal fissures. *Colorectal Disease*. 2012; 14(6): 760-4.
5. Garg P, Garg M, Menon GR. Long-term continence disturbance after lateral internal sphincterotomy for chronic anal fissure: a systematic review and meta-analysis. *Colorectal Disease*. 2013; 15(3): e104-17.
6. Sajid MS, Whitehouse PA, Sains P, Baig MK. Systematic review of the use of topical diltiazem compared with glyceryl trinitrate for the nonoperative management of chronic anal fissure. *Colorectal Disease*. 2013; 15(1): 19-26.
7. Nelson RL, Thomas K, Morgan J, Jones A. Non-surgical therapy for anal fissure. *Cochrane database of systematic reviews*. 2012(2).
8. Yiannakopoulou E. Botulinum toxin and anal fissure: efficacy and safety systematic review. *International journal of colorectal disease*. 2012; 27(1): 1-9.
9. Soltany S, Hemmati HR, Toussy JA, Salehi D, Toosi PA. Therapeutic properties of botulinum toxin on chronic anal fissure treatment and the patient factors role. *Journal of Family Medicine and Primary Care*. 2020; 9(3): 1562.

10. Akalin Ç, Yavuzarslan AB, Akyol C. Efficacy and Safety of Endoanal Ultrasound–Guided Botulinum Toxin in Chronic Anal Fissure. *The American Surgeon*. 2021; 00031348211034750.
11. Amorim H, Santoalha J, Cadilha R, Festas MJ, Barbosa P, Gomes A. Botulinum toxin improves pain in chronic anal fissure. *Porto Biomedical Journal*. 2017; 2(6): 273-6.
12. Brisinda G, Chiarello MM, Crocco A, Bentivoglio AR, Cariati M, Vanella S. Botulinum toxin injection for the treatment of chronic anal fissure: uni-and multivariate analysis of the factors that promote healing. *International Journal of Colorectal Disease*. 2022; 37(3): 693-700.
13. Ravindran P, Chan DL, Ciampa C, George R, Punch G, White SI. High-dose versus low-dose botulinum toxin in anal fissure disease. *Techniques in Coloproctology*. 2017; 21(10): 803-8.
14. Gulcu B, Ozturk E. Botulinum toxin injection is an effective alternative for the treatment of chronic anal fissure. *Acta Chirurgica Belgica*. 2021; 7: 1-7.
15. Dat A, Chin M, Skinner S, Farmer C, Wale R, Carne P, Bell S, Warriar SK. Botulinum toxin therapy for chronic anal fissures: where are we at currently?. *ANZ journal of surgery*. 2017; 87(9): E70-3.
16. Barbeiro S, Atalaia-Martins C, Marcos P, Gonçalves C, Canhoto M, Arroja B, et al. Long-term outcomes of Botulinum toxin in the treatment of chronic anal fissure: 5 years of follow-up. *United European gastroenterology journal*. 2017; 5(2): 293-7.