The Use of Nitroglycerin Ointment in the Treatment of Anal Fissures

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Abstract

Purpose: Comparing nitroglycerin ointment and other modalities of treatment like anal dilatation by four fingers under general anaesthesia, lateral sphincterotomy of the internal anal sphincter muscle, botulinum toxin injection, calcium channel blockers ,....etc in regard to patients compliance, healing rate, symptomatic relief, side effects and cost .

Methods: 48 patients , 29(60%) were males and 19(40%) were females had been studied prospectively after receiving a two weeks course of 0.2% nitroglycerin ointment every 6 hours, stool softeners and simple analgesia. The patients had been followed up in the outpatient clinic and the response to the treatment, regarding healing of fissures and relief of symptoms has been recorded.

Results: 28(58%) of the patients had symptomatic relief and good healing of their fissures and 20(42%) had poor healing. 10(50%) of the poor healers had symptomatic relief 36(75%) of the patients needed no subsequent surgery. None of the patients had side effects to the treatment.

Conclusion: Nitroglycerin ointment is a safe and effective method for the treatment of anal fissures with high healing rate and symptomatic relief together with low cost and minimal side effects leading to the high level of compliance of the patients.

الخلاصه

يعتبر الفطر الشرجي واحد من اكثر المشاكل الشرجيه شيوعا في مجتمعنا. خلال السنوات القليله الماضيه حاول العلم ايجاد علاجات مختلفه تهدف الى تقليل قوه العضلات الشرجيه العاصره حتى يشفى الفطر وهذه الطرائق العلاجيه تتنوع من توسيع الشرج بواسطه الاربع اصابع وهذه عمليه جراحيه تحت التخدير العام، ايضا القص الجانبي للعضله العاصره، حقن ماده سم البوتليتم، اعطاء عقاقير غالقه لقنوات الكالسيوم الى اخره من علاجات ومحاولات. وعليه فان ٠,٢% من مرهم النايترو جليسيرين يتميز بعده ميزات كونه رخيص نوعا ما ومتوفر في متناول المرضى ومعدلات الشفاء بواسطته جيده فضلا عن قله الاعراض الجانبيه الناتجه عن استخدامه.

في هذه الدراسه المجراة على ٤٨ مريض؛ ٢٩(٦٠%) من العينه كانوا من الذكور و ١٩ (٤٠%) كانوا من الاناث تمت دراسه حالاتهم ومتابعتهم بعد الاستمرار مده اسبوعين على العلاج ب ٠,٢% مرهم نايتروجلسيرين كل ٦ ساعات مع مسهلات مع عقاقير مسكنه بسيطة. وقد تمت متابعه المرضى في العياده الخارجيه ووجد ان استجابتهم للعلاج بالنسبه للشفاء واختفاء الاعراض هي كالتالي: ٢٨(٥٨%) من المرضى تماثلو للشفاء وتلاشت اعراض المرض، ١٤(٤٢%) كان شفاؤهم متعثر،٧(٥٠%) من المتعثر شفاؤهم اختفت عندهم الاعراض (الالام المبرحه). ٣٦(٧٥%) من المرضى لم يكونوا بحاجه للخضوع الى عمليه جراحيه واخيرا لم يشكو اي من المرضى من اي اعراض جانبيه من الدواء.

Introduction

Anal fissure is a breech in the distal anal mucosa [1-4]. Anal fissures lasting more than six weeks are considered chronic while those lasting less than six weeks are considered acute [5-8]. The etiology behind the anal fissure remains uncertain

but hypertonia and increased resting anal sphincter pressure are thought to be the cause [9,2-4]. This hypertonia of the anal sphincter muscles will cause ischemia of the mucosa of the anal canal [10-12]. However anal fissures can occur in the presence of normal or decreased anal muscle tone in exceptional cases especially in women following labour and in the elderly [13]. These post labour fissures are thought to be due to direct injury imposed to the anal mucosa especially on forceps delivery. There are many modalities of treatment of anal fissures both surgical and non surgical all are based on the notion of lowering the pressure of the internal anal sphincter muscles and here are some examples:

A. non surgical methods:

1. 0.2% nitroglycerin ointment it is thought to be a donor of nitrous oxide to the smooth muscles of the anal sphincters which is a relaxant neurotransmitter to these muscles and so promotes healing of the fissure by improving blood supply to the fissure area [14-16].
2. Calcium channel blockers: given both orally and locally. It acts by decreasing intra cellular calcium concentration and thus reducing intra cellular calcium availability to the myosin muscle fibers and then reducing the resting pressure of the internal anal sphincter and thus promoting fissure healing [17].
3. Angoitensin converting enzyme inhibitors [18 , 19].
4. Alpha blockers [20, 21].
5. Botulinum toxin injection [22-27].
6. Potassium channel openers e.g. Minoxidil [28].

B. surgical methods:

1. Four fingers dilatation: first performed in 1838 [29] and the technique had been reported to cause healing in 90% of patients [30].
2. Lateral internal sphincterotomy: has become the gold standard for surgical treatment of anal fissures due to the high healing rate and low risk of incontinence [31-34].
3. Fissurectomy: removing the fissure by scissors or diathermy. Apart from children it is not used alone as a treatment modality [27].
4. Advancement flap: recommended in patients with chronic fissures and normal or hypotonic anal sphincters especially in those with postpartum fissures or previous injury to the sphincter [35].

Patients and Methods

48 patients with anal fissures had been studied as outpatient and given a two weeks treatment course of 0.2% GTN ointment every 6 hours with stool softeners and analgesia (NSAID). Then the patients had been examined after completing their treatment course and recording the severity of symptoms and the healing of fissure after treatment. GTN ointment is not available as a ready made formula and it is usually manufactured locally by the local pharmacies.

Results

48 patients with acute anal fissures had been studied prospectively in the period between February 2008 and January 2009 after receiving treatment with GTN ointment simple analgesia and stool softeners.

97% of the patients presented with pain on defecation, 70% with constipation and 20% with anal bleeding on defecation.

29(60%) were males and 19(40%) were females. Mean age of patients was 33

(range 5-70) years. 33(69%) of the patients had posterior fissures while 15(31%) had anterior fissures.
33(69%) had acute fissures while 31% had chronic fissures.
26(54%) of the patients had secondary school and university education while the others were either illiterate or had primary school education.
28(58%) had good healing of their fissures and symptomatic relief 2 weeks after treatment and 14(42%) had poor healing. 7 (50%) of those patients with poor healing had good symptomatic relief (pain and bleeding).
None of our patients had side effects to the treatment.
36(75%) of the patients had good response to the treatment and needed no surgery following the treatment course and only 12(25%) needed subsequent surgery.

Discussion

In the presented study we found many advantages gained when using GTN ointment:
First was the availability of the medication since it is being locally made by most pharmacies using nitroglycerin tablets and Vaseline ointment.
Second was the compliance of the patients (89%). As they found it easy for them to use the ointment avoiding the complications of anesthesia and incontinence accompanying surgery of any kind [36-39].
Third was the cheap price of the medication costing about 10$ for a two weeks course while botulinum toxin treatment would cost about 200$ for one injection because the 100 units vial would cost this price though we use only 40 units for each session but the rest of the vial had to be discarded after use [35]. Surgery costs certainly more than GTN ointment treatment and the costs are variable.
Fourth was the low incidence of side effects. In fact we reported no side effect following the use of GTN ointment. Other studies stated headache following the use of GTN ointment [40,41]. In such case the severity of the headache would certainly be less than the pain caused by the anal fissure itself and it would be relieved by simple analgesia.
Fifth was the high cure rate after using a safe, readily available and acceptable treatment to most patients which was 75%.
GTN ointment should be the first resort for the treatment of patients with anal fissure in order to avoid the anesthetic complications of surgery and the variable risks of incontinence [36-39] although the cure rate is higher than GTN ointment approximating 90-95% [30,40-42].
Also the trail of using botulinum toxin was faced by the problems of high price and complications of anal sepsis, incontinence and perianal haematoma [43-45].

Conclusion

Nitroglycerin ointment is a safe and effective method for the treatment of anal fissures with high healing rate and symptomatic relief together with low cost and minimal side effects leading to the high level of compliance of the patients.

References

1. Sailer M, Bussen D, Debus ES, Fucks KH, Thiede A (1998). Quality of life in patients with benign anorectal disorders, Br J Surge 85: 1716-1719.
2. Utzig MJ, Kroesen AJ, Buhr HJ (2003). Concepts in pathogenesis and treatment of chronic anal fissure: a review of the literature Am J Gastroenterology 98: 968-974.
3. Schcouten WR, Briel JW, Auwerda JA, et al (1996). Ischemic nature of anal fissure, Br J Surge. 83: 63-65.
4. Gibbons CP, Read NW. (1986) anal hypertonia in fissures: cause or effect? Br J Surge 73: 443-45.
5. Griffen N, Acheson AG, Tong P, Sheard C, (2003). American gastroenterological association medical position statement: diagnosis and care of patients with anal fissure, gastroenterology 124: 233-234.
6. Lindsey I, Jones OM Cunningham C Mortensen NJ (2004). Chronic anal fissure , Br J Surg. 91 : 270-279.
7. Lock MR, Thomson JS (1977). Fissure in ano : the initial management and prognosis , Br J Surg. 64 : 355-358.
8. Lund JN, Scholefield JH (19960). Etiology and treatment of anal fissure , Br J Surg. 83: 1335- 1334
9. Brodie BC (1835). Lectures on diseases of the rectum , London Medical Gazette 16: 26-31
10. Anthony A (1999). Vascular anatomy in gastrointestinal inflammation , J Clin Pathol 52 : 381-384
11. Lund JN, Binch C, McGrath J, Sparrow A, Scholefield LH (1999). Topographical distribution of blood supply to the anal canal , Br J Surg 86 : 496-498
12. Schouten WR, Briel JW, Auwerda JA (1994). Relationship between anal pressure and anodermal blood flow , Dis Colon Rectum 37 : 664-669
13. Madoff RD, Steele SR (2006). Anorectal manometry and fissure treatment : author reply, Aliment pharmacol Ther 24 1652
14. Rattan S, Chakder S (1992). Role of nitric oxide as a mediator of internal sphincter relaxation , Am J Physiol 262 : G107 – G112
15. Rattan S, Sarkar A, Chakder S (1992). Nitric oxide pathway in rectoanal inhibitory reflex of opossum internal anal sphincter, Gastroenterology 103 : 43-50
16. Okelly TJ, (1996). Nerves that say NO: a new perspective on the human rectoanal inhibitory reflex , Ann R Coll Surg Engl 78 : 31- 38
17. Chrysos E , Xynos E , Tzovaras G , Zoras OJ , Tsiaoussus J , Vassilakis SJ (1996). Effect of nifedipine on rectoanal motility , Dis Colon Rectum 39 : 212-216
18. De Godoy MA, Dunn S, Rattan S (2004). Evidence for the role of angiotnsin 2 biosymthesis in the rat internal anal sphincter tone , Gastroentrology 127 : 127-138
19. Khaikin (2007) .Topical captopril cream: a new treatment for anal fissure? The first human study , Dis Colon Rectum 50 747
20. Yamato S , Rattan S (1990). Role of alpha adrenoceptors in opossum internal anal sphincter , J Clin Inves 86 : 424 – 429
21. Pitt J , Crags MM , Henry MM , Boulos PB (2000). Alpha 1 adrenoceptor blockade : potential treatment for anal fissures , Dis Colon Rectum 43: 800-803
22. Maria G, Casseta E, Gui D, et al (1998). A comparison of botulinum toxin and saline for the treatment of chronic anal fissure, M Engl G Med 338: 217-220.
23. Brizonda G, Maria G, Benti Voglio AR et al (1999). A comparison of

injections of botulinum toxin and topical GTN of the treatment of chronic anal fissure M Engl G Med 341: 65-69.
24. Arraoyo A, Perez F, Serrano P, et al (2005). Long term results of botulinum toxin for the treatment of chronic anal fissure: prospective clinical and manometric study, Int. J Cholorectal Dis. 20 : 267-271.
25. Lindsey I, Jhones OM, Cunningham C, et al (2003). Botulinum toxin as second line therapy for chronic anal fissure failing nitroglycerin ointment, Dis Colon Rectum 46: 361-366.
26. Silary P, Mele A, Stolfi VM, et al (2007). Medical and surgical treatment of chronic anal fissure: A prospective study J gastro intest Surge 11: 1541-1548.
27. Scholtz T, Hetzer FH, Dindo D et al (2007). Long term follow up after combined fissurectomy and botox injection for chronic anal fissure, Int J Cholorectal Dis: 1077-1081.
28. Muthurkumarassamy R, Robinson SS, Sarath SC, Raveendran R, (2005). Treatment of anal fissure using a combination of Minoxidil and lignocaine: A randomized, double blind trial, Indian J Gastro introl 24: 158-160.
29. Recamier JC, (1838). Extension, message et percussion cadancee dans les treatment des contractures musculaires , Rev Med Fr Estrang 1: 74
30. Marby M, Alexander-Williams J, Buchmann P et al (1979). A randomized controlled trial to compare anal dilatation and lateral subcutaneous sphincterotomy for anal fissure 22: 308-311
31. Bailey RV, Rubin RJ, Salvati EP (1978). Lateral internal sphincterotomy , Dis Colon Rectum ,21 : 584-586
32. Argov S, Levandovsky O (2000). Open lateral sphincterotomy is still the best treatment for chronic anal fissure , Am J Surg , 197 : 201-202
33. Hananel N, Gordon PH (1997). Lateral internal sphincterotomy for fissure in ano revisited , Dis Colon Rectum , 40 : 597- 602
34. Nelson RL (1999). Meta analysis of operative techniques for fissure in ano , Dis Colon Rectum , 42 : 1424- 1428
35. Jonas M, Scholefield JH (2001). Anal fissure , Gastroentrol Clin North Am 30 : 167-181
36. Saad AM, Omer A (1992). Surgical treatment of chronic fissure in ano : a prospective randomized study , East Afr Med J 69 : 613-615
37. Jensen SL, Lund F, Nielsen OV, Tange G (1984). Lateral subcutaneous sphincterotomy versus anal dilatation in the treatment of fissure in ano in outpatients : a randomized study , Br Med J (Clin Res Ed) 289 : 528-530
38. Goligher JC (1984). Surgery of the anus , rectum and colon , Bailliere Tindall , London
39. Melange M, Colin JF, Van Wymersch T, Van heuverzwyn R (1992). Anal fissure : correlation between symptoms and manometry before and after surgery , Int J Colorectal Dis 7 : 108- 111
40. Wiley M, Day P, Rieger N, Stephens J, Moore J (2004). Open versus closed lateral internal sphincterotomy for ideopathic fissure in ano : a prospective , randomized , controlled trial , Dis Colon Rectum 47 : 847-852
41. Garcea G, Sutton C, Mansoori S, Lloyd T, Thomas M (2003). Results following conservative lateral sphincterotomy for the treatment of chronic anal fissures , Colorectal Dis 5 : 311
42. Mentes BB , Irkorucu O , Akin M , Leventoglu S , Tatlicioglu E (2003) .Comparison of botulinum toxin

injection and lateral internal sphincterotomy for the treatment of chronic anal fissure , Dis Colon Rectum 46 : 232- 237
43. Jost WH,(1993) Use of botulinum toxin in anal fissure, Dis Colon Rectum 36: 974
44. Smith M, Frizelle F, (2004). Long term faecal incontinence following the use of botulinum toxin, Colorectal Dis 6: 526-527.
45. Jost WH, Schanne S, Mlitz H, Schimrigk K, (1995). Perianal thrombosis following injection therapy into the external anal sphincter using botulinum toxin Dis Colon Rectum 38: 781.