Topical treatments for anal fissure

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Clinical question

How effective are topical treatments (calcium channel blockers [CCBs], nitrates, and vitamin E) for chronic anal fissures in adults?

Bottom line

Healing rates with topical nitroglycerin are roughly 60% versus 40% with placebo at 8 weeks. Topical CCBs are at least as good as nitroglycerin, with a lower risk of headache (7% versus 56%). Based on 1 RCT, topical vitamin E may be superior to nitroglycerin (86% versus 66% healed at 8 weeks).

Evidence

Five meta-analyses of RCTs from the past 10 years were identified.[1-5] Adjunctive treatments were usually unclear (often fibre therapy or dietary advice). Healing was defined based on examination findings or patient report. Results were statistically significant unless indicated.

- Calcium channel blockers (eg, 2% diltiazem ointment): In 3 systematic reviews (1 to 7 RCTs, 60 to 727 patients), at about 6 weeks, 78% to 82% of patients were healed with CCBs versus 33% to 42% with control; number needed to treat (NNT)=3 (1 of the 3 analyses was not statistically different).[1-3]
- Nitroglycerin (eg, nitroglycerin 0.2% to 0.4% ointment): In 17 RCTs (1063 patients), at 8 weeks,[1] 63% of patients were healed versus 38% placebo; NNT=4.
  -Other systematic reviews found efficacy to be about 50% versus 35% placebo.[2,3]
- Calcium channel blockers versus nitroglycerin: In 11 RCTs (770 patients), at 8 weeks, 79% of patients were healed with CCBs versus 65% with nitroglycerin.[1] Similar results were found in other systematic reviews[3-5] but were statistically different in only 1.[3]
  -In 10 RCTs (590 patients), 7% had headache with CCBs versus 56% with nitroglycerin.[1]
- Vitamin E: In 1 RCT (160 patients, twice daily treatment),[6] at 8 weeks, 86% were healed with vitamin E versus 66% with nitroglycerin; NNT=5. None stopped vitamin E owing to headache versus 18% with nitroglycerin.
- Limitations: Some reviews included pediatric populations or did not include all RCTs. Many RCTs were unblinded, underdosed nitroglycerin, or had unclear vitamin E doses.

Context

- Guidelines recommend topical CCBs.[7] Botulinum toxin injections and surgery are options for treatment failure, but fecal incontinence is possible.[7]
- For an 8-week treatment, compounded topical CCBs or nitroglycerin cost roughly $60 per 30 g (personal communication from Stacy Jardine, Clinical Pharmacist, Peace River Value Drug Mart in Peace River, Alberta; 2022). Commercially available vitamin E ointment costs about $10 per 50 g.[8]

Implementation

Anal fissures are commonly found in middle-aged adults and in children.[9] They are primarily diagnosed by clinicians, with symptoms including pain during or after passage of stool, rectal bleeding, and linear tear (with or without a sentinel tag).[10] Most fissures are at the midline. Fissures not in the midline should be investigated for secondary causes (eg, Crohn disease).[11] Differential diagnosis of severe anal pain includes fissure, thrombosed hemorrhoids, or perirectal abscess.[9] Rectal bleeding is not necessarily diagnostic of malignancy but requires assessment and consideration of other risks factors.[12]

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Competing interests
None declared

References

1. Jin JZ, Hardy MO, Unasa H, Mauiliu-Wallis M, Weston M, Connolly A, et al. A systematic review and meta-analysis of the efficacy of topical sphincterotomy treatments for anal fissure. *Int J Colorectal Dis* 2022;37(1):1-15. Epub 2021 Oct 4.
2. Nelson RL, Thomas K, Morgan J, Jones A. Non surgical therapy for anal fissure. *Cochrane Database Syst Rev* 2012;(2):CD003431.
3. Nelson RL, Manuel D, Gumienny C, Spencer B, Patel K, Schmitt K, et al. A systematic review and meta-analysis of the treatment of anal fissure. *Tech Coloproctol* 2017;21(8):605-25. Epub 2017 Aug 9.
4. Nevins EJ, Kanakala V. Topical diltiazem and glyceryl-trinitrate for chronic anal fissure: a meta-analysis of randomised controlled trials. *Turk J Surg* 2020;36(4):347-52.
5. Sajid MS, Whitehouse PA, Sains P, Baig MK. Systematic review of the use of topical diltiazem compared with glyceryltrinitrate for the nonoperative management of chronic anal fissure. *Colorectal Dis* 2013;15(1):19-26.
6. Ruiz-Tovar J, Llavero C. Perianal application of glyceryl trinitrate ointment versus tocopherol acetate ointment in the treatment of chronic anal fissure: a randomized clinical trial. *Dis Colon Rectum* 2022;65(3):406-12.
7. Wald A, Bharucha AE, Limketkai B, Malcolm A, Remes-Troche JM, Whitehead WE, et al. ACG clinical guidelines: management of benign anorectal disorders. *Am J Gastroenterol* 2021;116(10):1987-2008.
8. *Webber vitamin E first aid ointment*. Mississauga, ON: Walmart.ca; 2022. Available from: **https://www.walmart.ca/en/ip/webber-vitamin-e-first-aid-ointment/6000189067438**. Accessed 2022 Oct 7.
9. Lu Y, Kwaan MR, Lin AY. Diagnosis and treatment of anal fissures in 2021. *JAMA* 2021;325(7):688-9.
10. Dykstra MA, Buie WD. Anal fissures. *CMAJ* 2019;191(26):E737.
11. Gilani A, Tierney G. Chronic anal fissure in adults. *BMJ* 2022;376:e066834.
12. Del Giudice ME, Vella ET, Hey A, Simunovic M, Harris W, Levitt C. Systematic review of clinical features of suspected colorectal cancer in primary care. *Can Fam Physician* 2014;60:e405-15. Available from: **https://www.cfp.ca/content/cfp/60/8/e405.full.pdf**. Accessed 2022 Dec 9.

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