

EVIDENCE-BASED REVIEWS IN SURGERY

Does antibiotic therapy prevent fistula in-ano after incision and drainage of simple perianal abscess?

Mantaj S. Brar, MD
Feza Remzi, MD
Janindra Warusavitarne, BMed,
PhD*
Indraneel Datta, MD, MSc;
for the Evidence Based Reviews
in Surgery Group

*J. Warusavitarne is the external expert reviewer of this manuscript.

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Correspondence to:

I. Datta
Department of Surgery and Oncology
Cumming School of Medicine
University of Calgary
1004 8 Ave SE
Calgary AB T2G 0M4
datta.indraneel@gmail.com

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SELECTED ARTICLE

Ghahramani L, Minaie MR, Arasteh P, et al. Antibiotic therapy for prevention of fistula in-ano after incision and drainage of simple perianal abscess: a randomized single blind clinical trial. *Surgery* 2017;162:1017–25.

KEY POINTS ABOUT THE ARTICLE

Background: The development of a perianal fistula following incision and drainage of a perianal abscess is common and leads to a significant burden of symptoms for patients and the need for further surgical intervention. **Study objective:** To assess the role of postoperative antibiotics in the prevention of fistula in-ano after incision and drainage of perianal abscess. **Methods:** The authors conducted a randomized single-blind clinical trial in which patients were assigned to either 7 days of oral metronidazole and ciprofloxacin in addition to standard care or to standard care alone without any antibiotics after discharge from the hospital. **Results:** Patients in the antibiotics group ($n = 155$) had significantly lower rates of fistula formation than those in the group that received standard care alone ($n = 144$, $p < 0.001$). Both univariate and regression analyses indicated that postoperative antibiotics had a protective role against fistula formation. **Conclusion:** The authors conclude that postoperative antibiotics play an important role in preventing fistula development and advise a 7- to 10-day course of postoperative antibiotics. Given the short-term follow-up in this study, it is unclear whether routine antibiotic administrations will decrease fistula formation in the long term.

COMMENTARY

The treatment of abscess and fistula of cryptoglandular origin remains a relevant general surgery topic. Antibiotic use as an adjunct to incision and drainage of an abscess has been limited to patients with immunodeficiency or with clinical evidence of cellulitis. At the same time, most of the literature has focused on surgical management of fistulae; however, if we could prevent fistula formation, multiple surgeries to treat this vexing problem could be avoided.

This is the question posed by Ghahramani and colleagues,¹ who report the results of their randomized single-blind superiority trial of antibiotics to prevent the formation of fistula. The authors sought to include 150 patients in each arm of the study, which was based on a baseline rate of 32% and a detection rate of an absolute difference of 15%. Simple random sampling was performed the day of surgery: on 2 randomly

selected days of the 4 days of the week on which colorectal surgery was performed at the hospital patients were allocated to the treatment group, while on the opposite 2 days patients were allocated to the control group. Unfortunately, given this randomization scheme, it is possible that the surgeons were aware of the allocation of patients at the end of each week. Presumably this changed week to week; otherwise, treatment assignment may have been confounded by surgeon (assuming surgeons are assigned days of the week).

Both groups received standard treatment, and the treatment group also received postoperative antibiotics. Importantly, this was a single-blind study with no placebo, therefore the patients were aware of their treatment allocation. During the immediate postoperative period, a trained nurse verified participants' compliance with study medication, after which patients were seen by the attending surgeon, who would not question medication history to ensure blinded outcome assessment. The duration of follow up was 3 months, with monthly visits by the same attending surgeon. An intention to treat principle was used for all patients for whom follow-up data were available, resulting in an absolute risk reduction of 17% (number needed to treat [NNT] = 5.8; 31% v. 14%). This corresponds to a relative risk of 0.45 and a relative risk reduction of 55%. The completeness of follow-up in this study was excellent, with only 8 patients lost to follow-up.

This study is important as it is generalizable to most patients seen by general surgeons. The authors used appropriate inclusion criteria (age > 18 yr, diagnosis of perianal abscess without any similar previous complaints) and, more importantly, reasonable exclusion criteria (previous fistula operation, coexisting fistula, irritable bowel disease, anal cancer or trauma, radiation history, cellulitis, horseshoe abscess, immunodeficiency, diabetes, valvular heart disease, mechanical heart valve, pregnancy or lactation, spontaneous drainage, concurrent antibiotic use). There were more men than women in the study (73%), the average body mass index was 26, and the smoking rate was 32.8%. The smoking rate was higher than one would expect, but may reflect the local population and may be explained by the gender imbalance in the study population. However, smoking on its own was not an independent risk factor for fistula formation in the authors' analysis after adjusting for gender.

The main limitation of the paper was whether it answered the most clinically important outcome: the development of a fistula in-ano in the long term. It is questionable that this outcome was adequately assessed in the 3-month follow-up period; a 6- to 12-month follow-up period would have been much more conclusive as it would have ensured that complications were

not just deferred rather than avoided altogether. Another limitation was the lack of a placebo for the control group; however, the blinded surgeon was performing clinical outcome assessment, therefore the impact of a placebo effect, although unknown, is presumably small.^{1,2} Finally, we do not know if the 2 study groups were similar at the onset of the trial, as the baseline characteristics of study participants were not stratified by treatment group, as is customary in all randomized controlled trials.

This trial is interesting for several reasons. Given concerns of antibiotic resistance, the use of antibiotics in general is controversial in the absence of strong evidence of effectiveness. However, the fecal microbiome and its role in gastrointestinal diseases, including cancer and even surgical complications, is an evolving and exciting area of active research.³ Several studies have attempted to look at the bacteriology of anal fistula, and it has been a surprising finding that the fistula tract itself appears to be relatively free of bacteria.⁴ If this is indeed the case, one would presume that antibiotics may have no effect on the overall rate of fistula formation. However, a great deal about the pathogenesis and development of fistulas of cryptoglandular origin remains unknown. The study by Ghahramani and colleagues¹ does not address which patients would benefit most from antibiotic treatment, and in the era of antibiotic stewardship and resistant organisms one has to ponder whether treating all patients with antibiotics is an appropriate approach. However, given that fistulae can be quite difficult to treat, it can be argued that any intervention to reduce the risk of fistula formation is likely a good strategy. Interestingly, the rate of fistula development was much higher among men in this study, which raises the question whether gender (or possibly smoking status) modifies the effect of antibiotics; this possibility was not assessed in the authors' analysis.

In summary, the study by Ghahramani and colleagues¹ was a reasonably well-designed randomized trial assessing whether routine antibiotic therapy with ciprofloxacin and metronidazole after cryptoglandular abscess drainage would reduce subsequent fistula formation. Their results are promising, with their specific antibiotic regimen showing a significant reduction in fistula formation in the antibiotic group and the low NNT of 5.8. However, with only a 3-month follow-up period, we question whether routine antibiotic administration with proper perianal abscess drainage would decrease fistula formation in the long term.

Affiliations: From the Department of Surgery, St. Paul's Hospital, Vancouver, BC (Raval, Morris); and the Department of Surgery, University of Rochester Medical Center, Rochester, New York (Temple).

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Members of the Evidence Based Reviews in Surgery Group: Chad G. Ball, Nancy N. Baxter, Mantaj Brar, Carl J. Brown, Prosanto K. Chaudhury, Indraneel Datta, Sandra de Montbrun, Justin Dimick, Elijah Dixon, G. William N. Fitzgerald, Samantha Hendren, Lillian S. Kao, Andrew Kirkpatrick, Steven Latosinsky, Robin S. McLeod, Arden M. Morris, Jason Park, Timothy M. Pawlik, Manoj Raval, Kjetil Soreide, Malin Sund, Larissa Temple, Bas Wijnhoven, Desmond Winter.

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