
Antibiotics versus no antibiotic therapy for uncomplicated sigmoid diverticulitis: A meta-analysis

Willmar Jayve M. Añoso, MD and Omar O. Ocampo, MD

Abstract

Introduction Antibiotics have been used customarily in the treatment of uncomplicated diverticulitis since their introduction and have become the standard of care. The aim of this study is to compare the effectiveness of antibiotic therapy versus no antibiotic therapy in the treatment of uncomplicated sigmoid diverticulitis.

Methods An electronic search for randomized controlled trials comparing antibiotics versus no antibiotic therapy for uncomplicated diverticulitis was conducted. The outcomes considered were associated morbidity (abscess formation and sigmoid perforation); need for sigmoid colon resection, and recurrence of diverticulitis. The included studies were evaluated for risk of bias. Meta-analysis with Forest plot was performed using Review Manager Version 5.3.

Results Two trials, consisting of 1,151 subjects, were included in the meta-analysis. There was no difference in the risk of sigmoid perforation (RR 1.02, 95% CI 0.30, 3.49). Abscess formation and incidence of sigmoid resection were lower in the antibiotics groups (RR 2.24, 95% CI 0.51, 9.95 and RR 1.59, 95% CI 0.75, 3.36, respectively) but the differences were not significant. There was no difference in the recurrence of diverticulitis (RR 1.05, 95% CI 0.74, 1.48) between the two groups.

Conclusion There is no definite advantage in giving antibiotics to patients with uncomplicated diverticulitis. Not giving antibiotics may be an acceptable treatment option for patients with acute uncomplicated sigmoid diverticulitis.

Key words: diverticular disease, uncomplicated diverticulitis, conservative management, antibiotics, treatment

Diverticulitis refers to inflammation and infection associated with a diverticulum in the bowel. The sigmoid colon is the most common site.^{1,2} The

pathophysiologic mechanism underlying sigmoid diverticulitis is not well-understood. However, the long-held belief that colonic diverticulitis is caused by microperforation and bacterial infection has been challenged by the concept that diverticulitis may be a primary inflammatory process.³

Uncomplicated sigmoid diverticulitis is the presence of inflamed sigmoid colon diverticula in the absence of complications such as perforation leading to peritonitis, fistula formation, obstruction due to stricture, and/or bleeding. It is usually

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characterized by an acute onset of left lower quadrant abdominal pain and tenderness. Computed tomography findings include the presence of colonic diverticula with associated pericolic soft tissue stranding, colonic wall thickening, and/or phlegmon formation.¹

Most patients with uncomplicated diverticulitis in the sigmoid colon will respond to conservative treatment in an out-patient setting.^{1,2} Conservative treatment of mild colonic diverticulitis typically includes careful observation while placing the patient on a low-residue diet with broad-spectrum oral antibiotics.² In a small number of patients with a more serious presentation such as severe abdominal pain, tenderness, fever, and leukocytosis, in-hospital treatment with bowel rest and parenteral antibiotics is done.² The majority of patients with uncomplicated sigmoid diverticulitis improves with these conservative measures and recovers without surgery.^{2,4}

Antibiotics have been used customarily in the treatment of uncomplicated left-sided colonic diverticulitis and have become the standard of care. Recently, a Cochrane database review found contradictory results between two randomized controlled trials with regard to the use of antibiotics in the treatment of uncomplicated sigmoid diverticulitis.⁵ The DIABOLO trial investigated the cost-effectiveness of treatment with or without antibiotics for uncomplicated acute sigmoid diverticulitis showed no significant difference in full recovery between the two strategies.⁶ On the other hand, the AVOD study group showed antibiotic treatment neither accelerates recovery nor prevents complications or recurrence of diverticulitis.⁷

The aim of our study is to compare the effectiveness of antibiotic therapy versus no antibiotic therapy in the treatment of uncomplicated sigmoid diverticulitis. Specifically, it aims to compare the incidence of morbidity in terms of perforation and abscess formation, sigmoid resection, and recurrence. The study also compares the length of hospital stay and clinical signs between the two treatment strategies.

Methods

Trials that were included in the study are those comparing antibiotic therapy versus no antibiotic therapy for uncomplicated sigmoid diverticulitis published in English. Randomized controlled trials wherein the participants were diagnosed by CT scan

to be stages 1a and 1b according to the Modified Hinchey's classification or "mild" diverticulitis according to Ambrosetti's criteria were included. The trials should have determined at least one of the following outcomes: morbidity, specifically sigmoid perforation and abscess formation; incidence of surgical resection (sigmoidectomy or partial colectomy); and recurrence. Trials that also looked into length of hospital stay and abdominal pain and tenderness were considered.

All randomized clinical trials comparing antibiotics versus no antibiotic therapy in patients diagnosed with uncomplicated sigmoid diverticulitis were identified by conducting an electronic search of the databases from Cochrane Library, PubMed and Google Scholar using the following keywords: diverticular disease, uncomplicated diverticulitis, sigmoid diverticulitis, conservative management, antibiotics, treatment. A comprehensive hand search of reference lists of published articles and review articles was performed to ensure inclusion of all possible studies and to exclude duplicates. Included were articles published in English up to May 2017. Review articles, non-randomized trials, retrospective analyses, and abstracts were not considered.

All potential trials were screened according to the criteria specified in the research protocol. Three reviewers extracted data from each publication. The third reviewer served as the arbiter who resolved all discrepancies. The quality of included studies was assessed independently by three reviewers using the Cochrane Handbook for Systematic Reviews of Interventions criteria: random sequence generation, allocation concealment, blinding of the patient and the observer, blinding of outcome assessment, incomplete outcome data, and selective outcome reporting. The main comparison was stratified according to morbidity, incidence of surgery, recurrence and length of hospital stay.

The relative risk or risk ratio (RR) was the primary measure of treatment effect or adverse events, and 95 per cent confidence intervals (CI) for RR were calculated. Heterogeneity was assessed by Q-square (χ^2) and I-square statistics (I^2).^{8,9} The I^2 statistic indicated the degree of between-study or interstudy variability as opposed to within-study or intra-study variability. An I^2 value greater than 50% was considered as substantial heterogeneity.^{8,9} Studies were analyzed using the fixed-effects model; when heterogeneity was significant, the random-effects

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model described by DerSimonian and Laird was used.⁹ Meta-analysis using Forest plots was performed with Review Manager Version 5.3.

Results

The search strategy resulted in 491 studies from the online databases. After excluding duplicates and articles that did not meet the inclusion criteria, seven full texts were reviewed for eligibility. Five articles were excluded because they were not randomized trials, leaving two for inclusion in the meta-analysis as seen in Figure 1.

Two trials were included in the meta-analysis and their characteristics are summarized in Table 1. The two studies included a total of 1,151 participants - 571 in the no antibiotic group and 580 in the antibiotic

group. The AVOD and DIABOLO studies followed up their patients for 1 and 2 years, respectively. Both studies satisfied the criteria for assessment except for blinding of patients and personnel. Assessment of quality according to the Cochrane Collaboration's tool for assessing risk of bias summary for RCTs is reported in Figure 2.

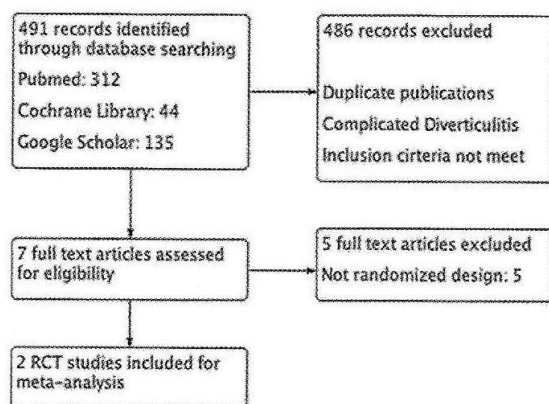


Figure 1. Study selection flowchart.

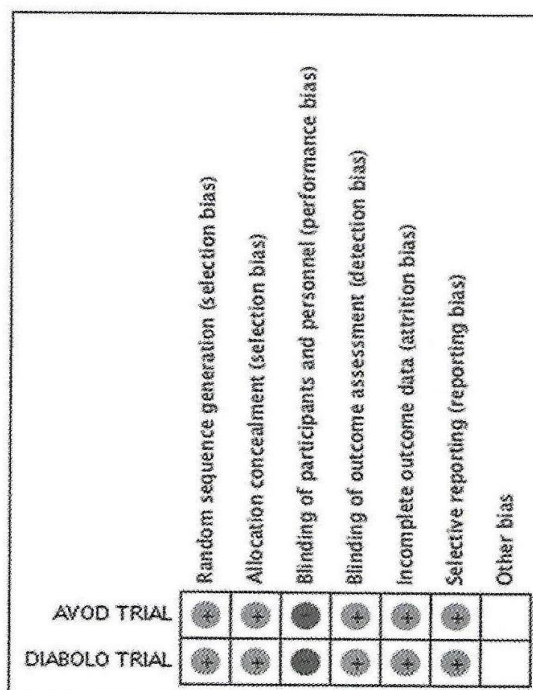


Figure 2. Risk of bias summary. (Gray - low risk of bias, Black - high risk, white - unclear)

Table 1. Summary of included studies.

Characteristic	AVOD trial, 2012 ⁶	DIABOLO trial, 2016 ⁷
Population	623	528
Follow up (months)	12	24
Antibiotics used	Cefuroxime / cefotaxime plus metronidazole, or carbapenem, or piperacillin-tazobactam, shifted to oral ciprofloxacin/ cefadroxil plus metronidazole	Amoxicillin-clavulanic acid IV shifted to oral
Outcomes	Complications (abscess formation, perforation), emergency surgery, hospital stay, recurrence	Recovery, days spent outside hospital (6 months), readmissions, complicated diverticulitis (abscess, perforation, obstruction/stricture, bleeding, fistula), ongoing diverticulitis, recurrence, need for resection/ surgery, other adverse events, mortality

Figure 3 demonstrates the incidence of sigmoid perforation between no antibiotics versus with antibiotics showing no statistical difference (overall effect $P = 0.98$). The incidence was 5 out of 566 subjects (0.88%) for the no antibiotics group versus 5 out of 575 subjects (0.86%) for the antibiotics group. The difference is not significant. As seen in Figure 4, abscess formation was seen in 5 out of 566 subjects (0.9%) for the no antibiotics group compared with 2 out of 578 subjects for the antibiotics group (0.3%). The overall risk ratio was 2.24 (95% CI, 0.51-9.95) and tends to favor the antibiotics group but is inconclusive.

The sigmoid was resected in 17 out of 554 subjects (3.0%) in the no antibiotics versus 11 out of 569 subjects (1.9%) in the antibiotics group. The risk ratio of 1.59 (95% CI, 0.75-3.36) tends to favor with antibiotics group but is inconclusive as seen in Figure 5. There was recurrence in 56 out of 552 subjects (10.1%) in the no antibiotics group compared with 54 out of 558 subjects (9.7%) in the antibiotics group. The overall risk ratio was 1.05 (95% CI, 0.74-1.48), indicating no statistical difference in recurrence between the antibiotics and no antibiotics group (Figure 6).

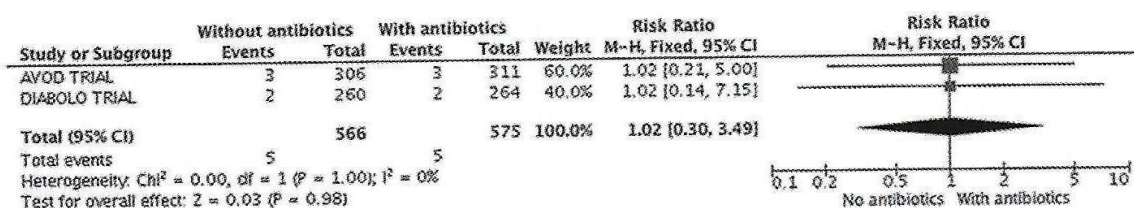


Figure 3. Comparison of sigmoid perforation between antibiotic and no antibiotic groups.

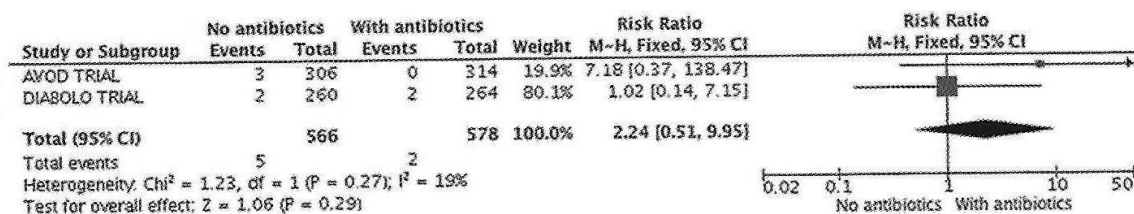


Figure 4. Comparison of incidence of abscess formation between antibiotic and no antibiotic groups.

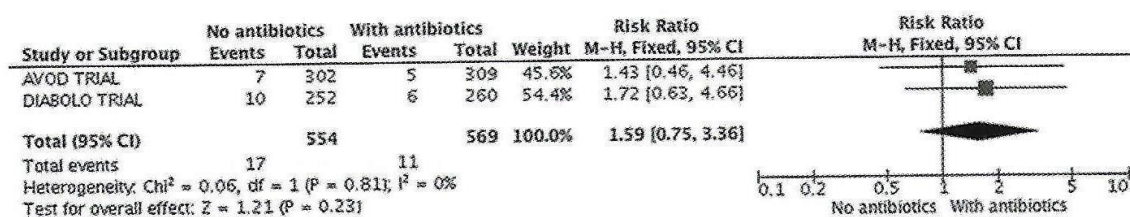


Figure 5. Comparison of incidence of sigmoid resection between antibiotic and no antibiotic groups.

The median length of hospital stay in both groups was comparable. In the AVOD trial, median length of hospital stay was 3 days in the no antibiotics group versus 3 days in the antibiotics group.⁷ Whereas in the DIABOLO trial, results demonstrated median length of hospital stay of 2 days in the no antibiotic group versus 3 days in the antibiotics group.⁶ Clinical bedside signs, such as abdominal pain, measured by VAS and tenderness on abdominal palpation at admission, did not differ between the groups.

Discussion

In this meta-analysis, treatment strategies using antibiotics versus no antibiotic therapy for uncomplicated sigmoid diverticulitis demonstrated no statistical difference between the two groups in terms of complications such as sigmoid perforation and abscess formation; incidence of sigmoid colon resection, and recurrence of diverticulitis. The risk ratio for patients who had undergone sigmoid colon resection (RR 1.59, 95% CI 0.75, 3.36) and patients who had abscess formation (RR 2.24, 95% CI 0.51, 9.95) tends to favor the antibiotic group, but is inconclusive.

Guidelines regarding treatment strategies for acute uncomplicated sigmoid diverticulitis have remained unchanged. According to Chabok, the recommendations for giving antibiotic therapy are based on tradition and expert opinions, and not on evidence derived from controlled clinical trials.⁷ Current guidelines have stated bowel rest or intake of oral fluids and a 7 to 10-day regimen of broad-spectrum antibiotics is recommended in patients with uncomplicated sigmoid diverticulitis.¹⁰⁻¹² Meanwhile, the likelihood that treatment of uncomplicated sigmoid diverticulitis may not require antibiotics was described and has been raised in literature.¹³ Two observational studies have also indicated that antibiotic therapy for uncomplicated sigmoid diverticulitis showed no benefit.^{14,15} Furthermore, two more retrospective cohort studies have indicated that a no-antibiotic policy for acute uncomplicated diverticulitis is feasible and safe.^{16,17}

The rationale behind treating an episode of uncomplicated left-sided colonic or sigmoid diverticulitis with antibiotics lies in the fact that it has long been believed that all forms of diverticulitis are the result of a colonic microperforation caused

by inspissated stool in a diverticulum. However, an overlap between diverticulitis and inflammatory bowel disease has long been recognized, and recent studies have postulated that all diverticular disease could be a form of inflammatory bowel disease.¹⁸ Altering the inflammatory response in cases of mild diverticulitis may be a more logical step than giving antibiotics.⁵

Antibiotic resistance has become a worldwide problem, and the use of antibiotics has other potential side effects such as nausea and vomiting, development of *Clostridium difficile* colitis, and fatal allergic reactions, among others.⁵ The possible development of such symptoms provides another important reason for reducing the frequent use of antibiotics in these patients.⁷ It could also be concluded that the risk of adverse effects and high costs warrant selective use whenever possible.¹⁴

A limitation of this study is the need for more randomized controlled studies comparing the use of antibiotics versus no antibiotics for acute uncomplicated sigmoid diverticulitis.

In this study, treatment strategies using antibiotics versus no antibiotic therapy for uncomplicated sigmoid diverticulitis demonstrated comparable results in terms of complications (sigmoid perforation, abscess formation), incidence of sigmoid colon resection, and recurrence. The risk ratio for patients who had undergone sigmoid colon resection and patients who had abscess formations tends to favor the antibiotic group, but is still inconclusive. Thus, there is no definite advantage in giving antibiotics to patients with uncomplicated diverticulitis. From these results, it may be postulated that not giving antibiotics may be an acceptable treatment option for patients with acute uncomplicated sigmoid diverticulitis.

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