Meta-analyses of Current Strategies to Treat Uncomplicated Diverticulitis

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BACKGROUND: Uncomplicated colonic diverticulitis is common. There is no consensus regarding the most appropriate management. Some authors have reported the efficacy and safety of observational management, and others have argued for a more aggressive approach with oral or intravenous antibiotic treatment.

OBJECTIVE: The purpose of this study was to perform an updated meta-analysis of the different management strategies for uncomplicated diverticulitis with 2 separate meta-analyses.

DATA SOURCES: MEDLINE, Embase, and Cochrane databases were used.

STUDY SELECTION: All randomized clinical trials, prospective, and retrospective comparative studies were included.

INTERVENTIONS: Observational and antibiotics treatment or oral and intravenous antibiotics treatment were included.

MAIN OUTCOME MEASURES: Successful management (emergency management, recurrence, elective management) was measured.

RESULTS: After review of 293 identified records, 11 studies fit inclusion criteria: 7 studies compared observational management and antibiotics treatment (2321 patients), and 4 studies compared oral and intravenous antibiotics treatment (355 patients). There was no significant difference between observational management and antibiotics treatment in terms of emergency surgery (0.7% vs 1.4%; $p = 0.1$) and recurrence (11% vs 12%; $p = 0.3$). In this part, considering only randomized trials, elective surgery during the follow-up occurred more frequently in the observational group than the antibiotic group (2.5% vs 0.9%; $p = 0.04$). The second meta-analysis showed that failure and recurrence rates were similar between oral and intravenous antibiotics treatment (6% vs 7% ($p = 0.6$) and 8% vs 9% ($p = 0.8$)).

LIMITATIONS: Inclusion of nonrandomized studies, identification of high risks of bias (selection, performance, and detection bias), and presence of heterogeneity between the studies limited this work.

CONCLUSIONS: Observational management was not statistically different from antibiotic treatment for the primary outcome of needing to undergo surgery. However, in patients being treated by antibiotics, our studies demonstrated that oral administration was similar to intravenous administration and provided lower costs. Although it may be difficult for physicians to do, there is mounting evidence that not treating uncomplicated colonic diverticulitis with antibiotics is a viable treatment alternative.

KEY WORDS: Antibiotics; Meta-analysis; Observational management; Uncomplicated colonic diverticulitis.

Colonic diverticular disease is frequent in developed countries and the most common GI-related cause for hospitalization in the Western world.[1] Up to 20% of patients with diverticulosis will report of symptomatic diverticulitis, of which 5% of cases present as complicated episodes (ie, perforation, peritonitis, obstruction, or bleeding). *Uncomplicated diverticulitis*, which is more common, is defined as a focal pain and tenderness in the left lower abdomen, associated with

Funding/Support: Dr Mege was supported by grants from the French Association of Surgery, French Society of Digestive Surgery, Foundation of Aix-Marseille University, and the Association for Development in Laboratory and Medical Searches, France.

Financial Disclosure: None reported.

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Dis Colon Rectum 2019; 62: 371–378
DOI: 10.1097/DCR.0000000000001295

leukocytosis and the absence of a complication on CT scan (ie, stricture, perforation, abscess, pneumoperitoneum, or peritonitis). Overall, the incidence of diverticulitis is increasing worldwide and is thought to be because of Westernization in many countries and an increase in a carbohydrate-rich and fiber-low diet. The overall prevalence of hospitalization for diverticulitis has increased from 74.1 per 100,000 persons in 2000 to 91.9 per 100,000 persons in 2010 in the United States.[2] Although the incidence of uncomplicated diverticulitis is increasing, there are several controversies that still remain in the management and care of these patients.

The traditional management of uncomplicated diverticulitis has been based on bowel rest or intake of oral fluids and a 7- to 10-day regimen of broad-spectrum antibiotics. Yet, in 2016, the World Society of Emergency Surgery guidelines stated that antimicrobial therapy can be avoided in immunocompetent patients with uncomplicated diverticulitis without systemic manifestations of infection (recommendation 1A), and if patients need antimicrobial therapy, oral administration may be acceptable (recommendation 1B).[3] Concurrently, a recent systematic review of randomized trials reported that mesalazine was more effective in obtaining symptom relief and in preventing recurrence in comparison with placebo and other therapies (antibiotics, probiotics, or high-fiber diet).[4] In spite of these recommendations, a recent expert international opinion reported that there is a lack of high-level evidence to support no use of antibiotics, with an agreement in only half of experts.[5]

As a result of the controversies surrounding the management of uncomplicated diverticulitis, we sought to perform an updated meta-analysis of all high-quality trials to help for the best course in management of uncomplicated colonic diverticulitis, with 2 separate meta-analyses, including, first, the analysis of observational versus antibiotics treatment and, second, in case of antibiotic treatment, the analysis of oral versus intravenous antibiotics treatment.

MATERIALS AND METHODS

This review uses the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines methodology.[6]

Criteria for Considering Studies for This Review

In conjunction with a trained librarian, we performed a systematic review to select our studies for analysis. For the meta-analysis, we included all randomized controlled trials and comparative prospective and retrospective studies that addressed the medical management of uncomplicated diverticulitis. Trials fell under 2 categories, those that compared observational and antibiotic treatment or oral and intravenous antibiotic treatment in the management of uncomplicated colonic diverticulitis.

Patients were included if they had acute uncomplicated colonic diverticulitis (including modified Hinchey I a), confirmed by a CT scan. Patients with complicated colonic diverticulitis (modified Hinchey I b or more) were not included in this analysis. Two separate meta-analyses were performed, including analysis between observational and antibiotic treatment and analysis between oral and intravenous antibiotics treatment in the presence of antibiotic treatment.

The intervention group included all of the patients with confirmed diverticulitis who received no antibiotic treatment (for the first analysis) or oral antibiotics (for the second analysis). The control group was any patient with diverticulitis treated with either oral or intravenous anti-

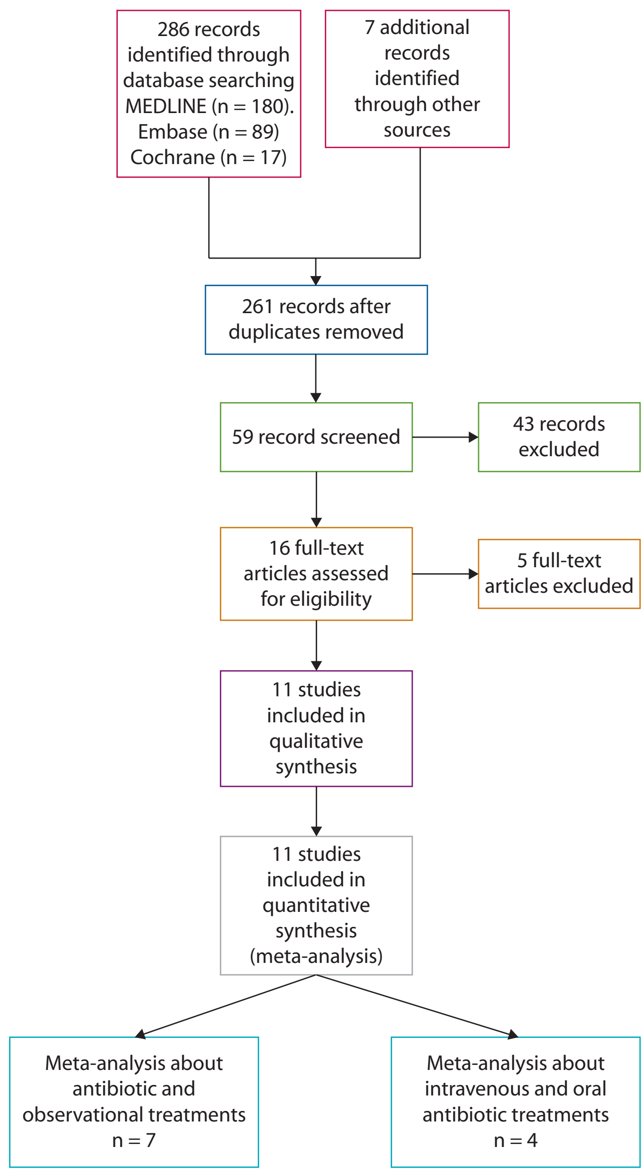

FIGURE 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flow chart of literature search.

TABLE 1. Characteristics of included studies comparing antibiotics and observational treatment

References	Type of study	Sample size	First episode, n (%)	Intervention	Outcomes	Follow-up
Papi et al[8]	RCT	168	NA	Rifaximin vs placebo	Symptom score, recurrence	12 mo
Hjern et al[17]	Retrospective case series	311	224 (72)	Cephalosporin/ Ciprofloxacin + metronidazole vs fluids	Recovery, emergency surgery, recurrence, elective surgery	30 mo (range, 16–45 mo)
de Korte et al[18]	Retrospective case series	272	NA	Piperacillin + metronidazole or amoxicillin–clavulanic acid vs fluids	Recovery, emergency surgery, recurrence, elective surgery	50 mo (range, 12–100 mo)
Chabok et al[9]	RCT	623	368 (59)	Cephalosporin + metronidazole or carbapenem or piperacillin–tazobactam vs fluids	Symptom score, complications, emergency surgery, recurrence, elective surgery	12 mo
Isacson et al[16]	Retrospective case series	195	NA	Antibiotics vs fluids	Recovery, emergency surgery, recurrence, elective surgery	12 mo
Brochmann et al[15]	Retrospective case series	224	169 (75)	Antibiotics vs fluids	Complications, Emergency surgery, Recurrence, Elective surgery	12 mo
Daniels et al[10]	RCT	528	528 (100)	Amoxicillin–clavulanic acid or ciprofloxacin + metronidazole vs fluids	Recovery, emergency surgery, recurrence, elective surgery	12 mo

RCT = randomized controlled trial; NA = not available.

biotics (for the first analysis) and only intravenous antibiotics (for the second analysis).

Primary outcome was treatment failure as defined by a need for emergent surgery. Emergent surgery was performed for a complication, including bowel perforation with free air, abscess, or fistula.

Secondary outcomes were length of stay, rates of elective surgery during the follow-up, and recurrence. Elective surgery was performed out of emergency for symptomatic diverticular disease with stricture, fistula with another organ, or repetitive recurrences. *Recurrence* was defined as readmission for a new episode of acute diverticulitis 1 month after the previous case.

Search Methods for Identification of Studies

In conjunction with an academic librarian, an electronic search was performed through MEDLINE, Embase, and Cochrane Database of Systematic Reviews, between 1981 and 2017, using a combination of key search terms: *colonic diverticulitis* OR *diverticulitis* AND *uncomplicated*. Only publications in English were included.

A total of 286 records were identified through database searches, and 7 additional records were identified by a hand search of reference lists from identified studies and systematic reviews.

Data Collection and Analysis

One author (D.M.) reviewed titles and abstracts of the screened studies. When studies could not be excluded on the basis of title and abstracts, full texts were reviewed. The search strategy was illustrated in the PRISMA flow chart (Fig. 1). As per guideline standards, noncomparative studies were not included.

One author (D.M.) extracted data from each study. The included studies and extracted data were reviewed and confirmed by a second author (H.Y.). Extracted data included demographic characteristics and posttreatment outcomes (readmission or surgery).

Statistical Analyses

The statistical software Review Manager 5.3 (The Cochrane Collaboration, Copenhagen, Denmark) was used.

TABLE 2. Characteristics of included studies comparing intravenous and oral antibiotics treatment

References	Type of study	Sample size	First episode, n (%)	Intervention	Outcomes	Follow-up
Ribas et al[12]	RCT	44	34 (77)	Amoxicillin–clavulanic acid intravenous vs oral	Failure, emergency surgery, cost	2 mo
Park et al[13]	Prospective case series	103	103 (100)	Cephalosporin + metronidazole intravenous vs oral	Failure, recurrence, cost	21 mo (range, 4–40 mo)
Moya et al[14]	Prospective case series	76	62 (82)	Ciprofloxacin + metronidazole intravenous vs oral	Failure, emergency surgery, recurrence, cost	7–9 mo
Biondo et al[11]	RCT	132	NA	Amoxicillin–clavulanic acid intravenous vs oral	Failure, emergency surgery, quality of life, cost	2 mo

RCT = randomized controlled trial; NA = not available.

TABLE 3. Characteristics of excluded studies

References	*Type of study*	*Sample size, n*	*Inclusion criteria*	*Intervention*
Ridgway et al[21]	RCT	79	Uncomplicated and complicated diverticulitis	Intravenous vs oral antibiotics
Ünlü et al[23]	Retrospective case series	312	Uncomplicated diverticulitis	Inpatient vs outpatient with or without antibiotics
Isacson et al[19]	Prospective cohort, no comparative	155	Uncomplicated diverticulitis	Fluids only
Mali et al[20]	Prospective cohort, no comparative	153	Uncomplicated diverticulitis	Fluids only
Sirany et al[22]	Retrospective case series	240	Uncomplicated and complicated diverticulitis	Inpatient vs outpatient with or without antibiotics

RCT = randomized controlled trial.

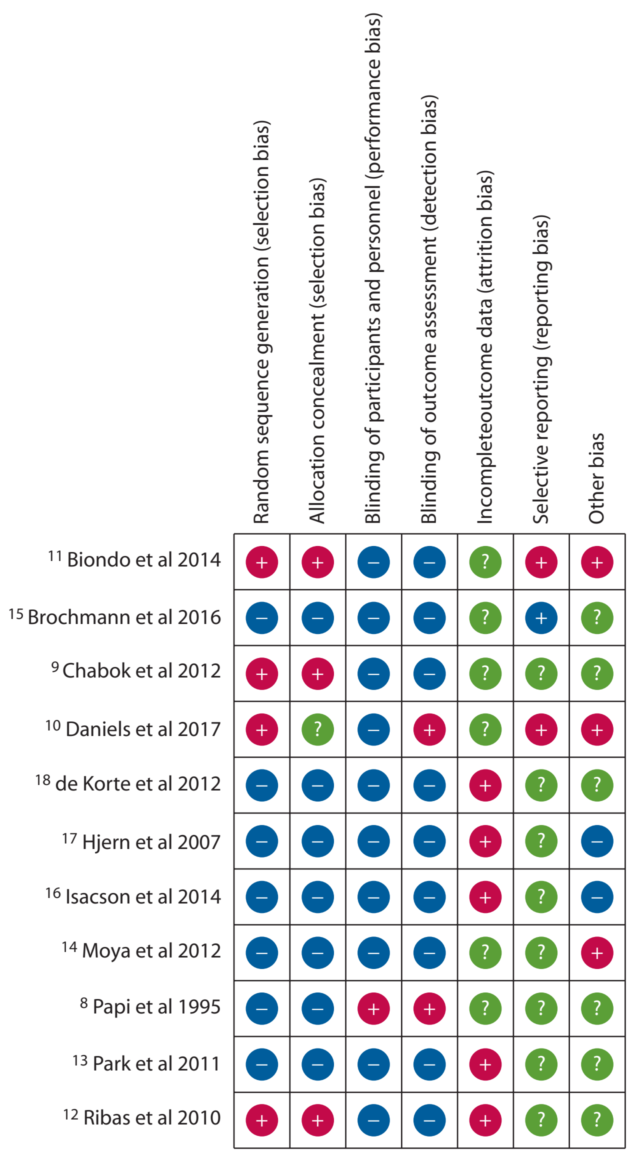

FIGURE 2. Risk of bias summary: review authors' judgments about each risk of bias item for each included study.

Two meta-analyses were performed, including observational versus antibiotics treatment and oral versus intravenous antibiotics treatment. ORs were calculated for dichotomous variables, indicating the relative benefits of observational management compared with antibiotic treatment. In case of missing outcomes, the authors of the included studies were contacted. Original authors were contacted for cost data, but because of the way that cost data were calculated in their studies and the heterogeneity, they could not be used for analysis in the larger data set.

Heterogeneity was assessed using a statistical test for heterogeneity ($p < 0.1$ was considered significant) or the I^2, according to Rhodes et al.[7] In the presence of heterogeneity, subgroup analysis was performed.

The quality of the included studies was assessed in relation to their risk of bias using the criteria described by the Cochrane Handbook of Systematic Reviews of Interventions. The risk of bias was evaluated as low, unclear, or high for the following areas: sequence allocation, allocation concealment, participant blinding, assessor blinding, follow-up completion, and selective reporting. Funnel plots were used to consider the potential for publication bias.

RESULTS

Description of Studies

Our search strategy is illustrated in the PRISMA flow chart (Fig. 1). Of 293 identified records, 16 full-text articles of potential relevance were identified, and of them 11 were definitively included. There were 5 randomized controlled trials[8–12] and 2 prospective[13,14] and 4 retrospective[15–18] comparative studies. The characteristics of included studies are reported in Tables 1 and 2.

Five studies were excluded because 2 of them were single-arm studies,[19,20] 1 included complicated diverticulitis,[21] and 2 others had heterogeneous interventions.[22,23]

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds ratio M - H, fixed, 95% CI
Brochmann et al[15]	0	177	0	47		Not estimable
Chabok et al[9]	1	309	3	314	20.7%	0.34 (0.03, 3.25)
Daniels et al[10]	2	262	3	266	20.6%	0.67 (0.11, 4.07)
de Korte et al[18]	6	191	3	81	28.5%	0.84 (0.21, 3.46)
Hjern et al[17]	0	193	3	118	30.2%	0.09 (0.00, 1.67)
Isacson et al[16]	0	178	0	17		Not estimable
Total (95% CI)		1310		843	100.0%	0.47 (0.20, 1.14)
Total events						

Heterogeneity $\chi^2 = 2.15, df = 3$ ($p = 0.54$); $I^2 = 0\%$
Test for overall effect: $Z = 1.66$ ($p = 0.10$)

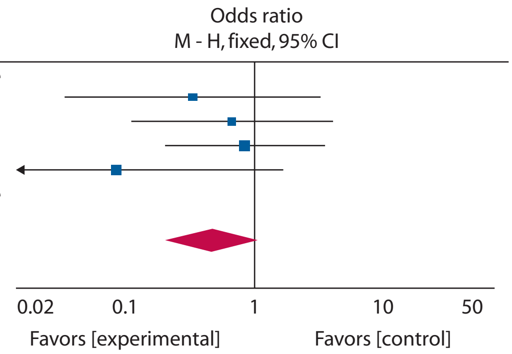

FIGURE 3. Forest plot of emergent surgery between observational and antibiotic treatments. M-H = Mantel–Haenszel; df = degrees of freedom.

The characteristics of excluded studies are reported in Table 3.

The risk of bias is reported in Figure 2. Because nonrandomized studies were included, high risks of bias were identified, whether selection, performance, or detection bias.

Effects of Interventions

Meta-Analysis 1: Observational Management Versus Antibiotics Treatment

Seven studies compared observational management and antibiotics treatment, including 3 randomized controlled trials[8–10] and 4 retrospective case series[15–18] (Table 1). A total of 2321 patients were included in these 7 studies; 1394 underwent observational management (60%), and 927 were under antibiotic treatment (40%). Antibiotics used varied among the studies but included rifaximin,[8] cephalosporin, and metronidazole[9,17] or amoxicillin–clavulanic acid.[10,18] In 2 studies, the type of antibiotics was not indicated.[15,16] The length of antibiotics use varied between 7 and 10 days in most of the studies,[8–10,18] and Hjern et al[17] reported 14 days. A total of 1289 patients presented with their first episode of uncomplicated diverticulitis (of 1686 total in available data (76%)).

Treatment failure was reported as the necessity of emergency surgery in 6 of the trials. Emergency surgery occurred less frequently in the observational group than in the treatment group (0.7% vs 1.4%), but the difference was not significant (OR = 0.47 (95% CI, 0.20–1.14); $p = 0.1$; participants = 2153; studies = 6; $I^2 = 0\%$; Fig. 3). Considering only randomized trials, a subgroup analysis was performed and confirmed that emergent surgery occurred less frequently in the observational group than in the treatment group (0.5% vs 1.0%), without significant difference (OR = 0.51 (95% CI, 0.13–2.03); $p = 0.34$).

Secondary outcomes were elective surgery in 6 studies and recurrence rates in all of the included studies. Elective surgery rates during the follow-up favored observational treatment, without demonstrating a significant difference (2.0% vs 2.5%; OR = 0.76 (95% CI, 0.43–1.36); $p = 0.4$; participants = 2153; studies = 6; $I^2 = 64\%$). Because there was significant heterogeneity among the studies, a subgroup analysis was performed, including only randomized controlled trials. In this subgroup analysis, elective surgery rates during the follow-up favored antibiotic treatment (2.5% vs 0.9%; OR = 2.89 (95% CI, 1.03–8.09); $p = 0.04$; participants = 1151; studies = 2; $I^2 = 0\%$; Fig. 4). Recurrence rates were similar between groups (11% versus 12%, OR = 0.86 (95% CI, 0.65–1.14); $p = 0.3$; participants = 2253; studies = 7; $I^2 = 8\%$; Fig. 5). The mean difference for length of stay was significantly in favor of observational management (–0.75 [range, –0.89 to –0.61); $p < 0.0001$), yet the included studies were significantly heterogeneous ($I^2 = 89\%$; $p < 0.0001$). The funnel plot did not suggest evidence of publication bias (Fig. 6).

Meta-Analysis 2: Oral Versus Intravenous Antibiotics

Four studies comparing oral and intravenous antibiotics treatment were included, 2 randomized controlled trials[11,12] and 2 prospective case series[13,14] (Table 2). The

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds ratio M - H, fixed, 95% CI
Chabock et al[9]	6	309	2	314	40.3%	3.09 (0.62, 15.42)
Daniels et al[10]	8	262	3	266	59.7%	2.76 (0.72, 10.52)
Total (95% CI)		571		580	100.0%	2.89 (1.03, 8.09)
Total events	14		5			

Heterogeneity. $\chi^2 = 0.01, df = 1$ ($p = 0.92$); $I^2 = 0\%$
Test for overall effect: $Z = 2.03$ ($p = 0.04$)

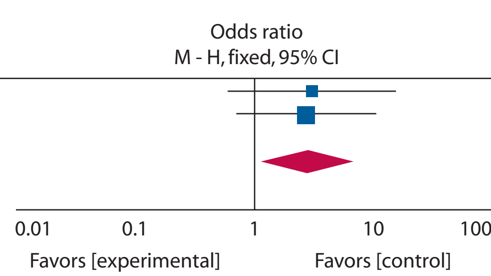

FIGURE 4. Forest plot of elective surgery without heterogeneity between observational and antibiotic treatments. M-H = Mantel–Haenszel; df = degrees of freedom.

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds ratio M - H, fixed, 95% CI
Brochmann et al[15]	8	174	5	46	7.1%	0.40 (0.12, 1.27)
Chabok et al[9]	47	290	46	292	36.1%	1.03 (0.66, 1.61)
Daniels et al[10]	9	262	8	266	7.2%	1.15 (0.44, 3.02)
de Korte et al[18]	14	191	12	81	14.7%	0.45 (0.20, 1.03)
Hjern et al[17]	51	186	32	115	27.0%	0.98 (0.58, 1.65)
Isacson et al[16]	21	178	4	17	6.1%	0.43 (0.13, 1.46)
Papi et al[8]	2	77	2	78	1.8%	1.01 (0.14, 7.38)
Total (95% CI)		1358		895	100.0%	0.86 (0.65, 1.14)
Total events	152		109			

Heterogeneity $\chi^2 = 6.52$, $df = 6$ ($p = 0.37$); $I^2 = 8\%$
Test for overall effect: $Z = 1.06$ ($p = 0.29$)

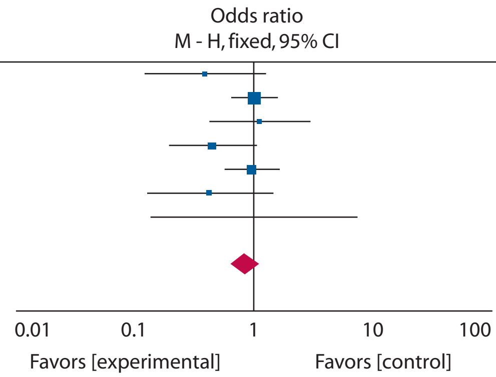

FIGURE 5. Forest plot of recurrence after observational and antibiotic treatments. M-H = Mantel–Haenszel; df = degrees of freedom.

meta-analysis analysis included 355 patients, of whom 199 presented with their first episode of uncomplicated diverticulitis (223 had complete data (89%)). Oral and intravenous antibiotic treatments were administered in 160 (45%) and 195 patients (55%). Antibiotics included in the studies were amoxicillin–clavulanic acid, cephalosporin, or ciprofloxacin with metronidazole. Failure rates were similar between oral and intravenous antibiotic treatments (6% vs 7%; OR = 0.76 (95% CI, 0.33–1.78); $p = 0.6$; participants = 355; studies = 4; $I^2 = 39\%$; Fig. 7).

Recurrence was reported in the 2 prospective case series.[13,14] Recurrence rates were similar between the 2 groups (8% vs 9%, OR = 0.88 (95% CI, 0.30–2.54); $p = 0.8$; participants = 181; studies = 2; $I^2 = 0\%$; Fig. 8).

DISCUSSION

This is the first meta-analysis with a large enough sample size to evaluate the role of antibiotics versus observation in immunocompetent patients with uncomplicated diverticulitis and the first to support recent international guidelines (recommendation 1 B).[3,24] These data support that observational treatment was not statistically different from antibiotic treatment for uncomplicated diverticulitis in terms of emergency surgery and recurrence. This study also shows that elective surgery is more likely to happen in patients who do not take antibiotics. For patients who do take antibiotics, oral and intravenous administration had similar failure and recurrence rates.

The pathogenesis of uncomplicated acute diverticulitis remains uncertain. Low-grade inflammation, altered intestinal microbiota, visceral hypersensitivity, and abnormal colonic motility have been identified as factors leading to symptom development.[25] A few authors considered that diverticulitis is a form of IBD and not the result of microperforation.[26,27] For these reasons, different treatments have been proposed to treat uncomplicated diverticulitis, including high-fiber diets, broad-spectrum antibiotics, probiotics, or 5-aminosalicylic acid (mesalazine, balsalazide).

The current increasing incidence of uncomplicated diverticulitis has led to a large medical burden, and the unnecessary use of antibiotics is a major cause of the emergence of resistant organisms. It can also be associated with *Clostridium difficile* superinfection or allergic reactions. To decrease costs and adverse effects, several authors have tried to demonstrate the efficacy of nonantibiotic treatment[8–10,15–20] or at least the oral administration of antibiotics through an outpatient setting.[11–14,21–23] Two meta-analyses, including 1 from Cochrane Library, failed previously to confirm these results because they included a small number of heterogeneous series with investigation of different interventions.[28,29] In our meta-analysis, we have included all of the comparative studies about treatment of uncomplicated diverticulitis, and we performed 2 groups of analyses, 1 for nonantibiotic management and another for oral administration. We were unable to analyze regarding other therapies, such as mesalazine or probiotics. Although several randomized controlled trials were published about these therapies, they were too heterogeneous to perform any meta-analysis. Some compared mesalazine with antibiotics (rifaximin)[30,31] and others with placebo[32] or probiotics.[33]

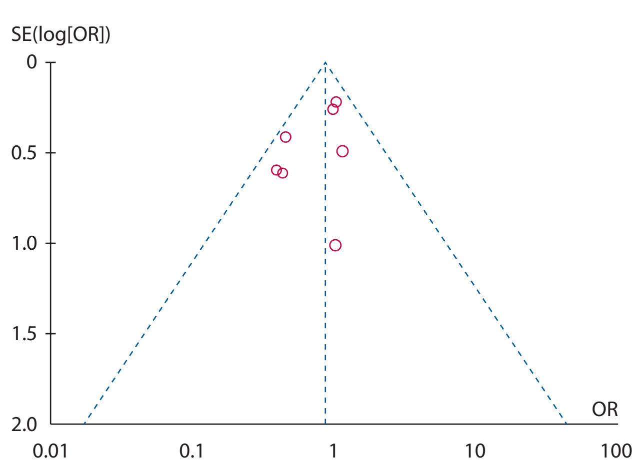

FIGURE 6. Publication bias analysis: funnel plot of comparison between observational and antibiotics treatments.

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds ratio M - H, fixed, 95% CI
Biondo et al[11]	3	66	4	66	31.3%	0.74 (0.16, 3.43)
Moya et al[14]	2	32	9	44	58.2%	0.26 (0.05, 1.29)
Park et al[13]	2	40	0	63	3.0%	8.25 (0.39, 176.35)
Ribas et al[12]	2	22	1	22	7.5%	2.10 (0.18, 25.01)
Total (95% CI)		160		195	100.0%	0.79 (0.34, 1.84)
Total events	9		14			

Heterogeneity $\chi^2 = 4.70, df = 3$ ($p = 0.19$); $I^2 = 36\%$
Test for overall effect: $Z = 0.56$ ($p = 0.58$)

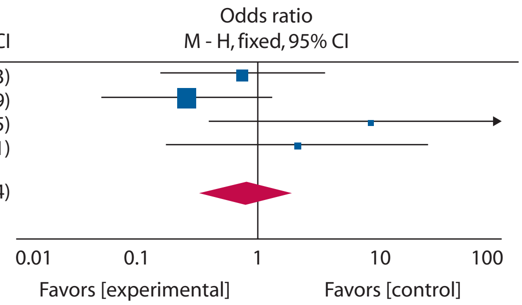

FIGURE 7. Forest plot of failure after oral and intravenous antibiotic treatments. M-H = Mantel–Haenszel; df = degrees of freedom.

We observed that emergency surgery occurred less frequently in the observational group than in the antibiotic treatment group, but the difference was not significant, and recurrence rates were similar between groups. Elective surgery during the follow-up favored observational treatment, without demonstrating a significant difference, with a significant heterogeneity between studies. A subgroup analysis has thus been performed with only randomized controlled trials, and the elective surgery rate was significantly higher in the observational group than in the antibiotic group (2.5% vs 0.9%; OR = 2.89 (95% CI, 1.03–8.09); $p = 0.04$). This result should be considered with caution, because the 2 randomized trials individually did not report a significant difference for elective resection, so our difference may be seen because of increased power of our study to detect a difference. Unfortunately, elective surgery was not clearly defined within the studies. Only Chabok et al[9] reported emergent surgery for complications and, separately, surgery during the follow-up for symptomatic diverticular disease, stricture, fistula, or recurrent diverticulitis. In addition, because most of the studies did not have long-term follow up (>12 mo), it is possible that some events may have happened later and as a result were left out of the analysis.

For patients receiving antibiotics, we noted that failure and recurrence rates were similar between oral and intravenous administration. Unfortunately, we were unable to perform a cost analysis because cost reported in the included studies was only an estimate for 1 patient, without statistical data.

This systematic review and meta-analysis had a number of limitations. Among the 11 included studies, only 5 were randomized controlled trials. Because we have included nonrandomized studies, a high risk of bias was identified, whether selection, performance, or detection bias. There is significant risk of allocation bias in the nonrandomized studies. It is possible that patients with less severe diverticulitis were allocated to treatment without antibiotics. Indeed, in the study by de Korte et al,[18] patients in the antibiotics group were more severe than those in observational management. It is also important, that, although we had strict selection criteria, there was significant heterogeneity between the studies, leading to subgroup analyses with only randomized controlled trials. We tried to limit this heterogeneity by exclusion of studies without evidence of uncomplicated diverticulitis[21] or in the case of intervention groups not clearly defined.[22,23]

Currently, observational management is not frequently practiced by clinicians, and these data suggest that we are overtreating patients. Because of physician reluctance to use this management, we should consider additional studies to help better identify which patients may be most likely to benefit from nonantibiotic management. For other patients, oral administration through an outpatient setting could reduce hospitalization costs. Additional studies may improve the real place of other therapies (mesalazine or probiotics) in the management of uncomplicated acute diverticulitis.

CONCLUSION

This review is the first meta-analysis to confirm the new international guidelines and to demonstrate that nonantibiotic management is not associated with increased emergency surgery. It is associated with shorter length of stay. Recurrence rates were not increased after observational

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds ratio M - H, fixed, 95% CI
Moya et al[14]	2	34	3	44	33.5%	0.85 (0.13, 5.42)
Park et al[13]	4	40	7	63	66.5%	0.89 (0.24, 3.25)
Total (95% CI)		74		107	100.0%	0.88 (0.30, 2.54)
Total events	6		10			

Heterogeneity $\chi^2 = 0.00, df = 1$ ($p = 0.97$); $I^2 = 0\%$
Test for overall effect: $Z = 0.24$ ($p = 0.81$)

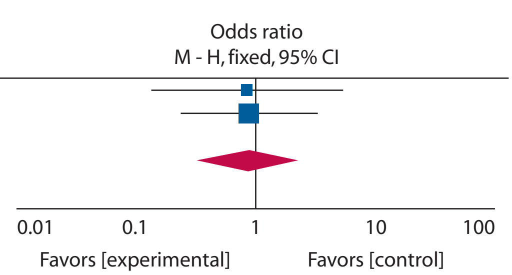

FIGURE 8. Forest plot of recurrence between oral and intravenous antibiotic treatments. M-H = Mantel–Haenszel; df = degrees of freedom.

management, whereas elective surgery occurred more frequently in the randomized trials. Physicians should consider this for patients. These results should be confirmed by additional randomized studies, with better definitions of outcomes and longer follow-up.

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