

Antibiotics for acute uncomplicated diverticulitis in hospitalized patients

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Citation Araya-Quezada C, Torres-Bavestrello L, Gómez-Barbieri G, Zárate-Castillo A. Antibiotics for acute uncomplicated diverticulitis in hospitalized patients. *Medwave* 2021;21(2):e8140

Doi 10.5867/medwave.2021.02.8140

Submission date 11/9/2020

Acceptance date 1/3/2021

Publication date 26/3/2021

Origin Not commissioned

Type of review Externally peer-reviewed by two reviewers, double-blind

Keywords acute uncomplicated diverticulitis, antibiotics, observational treatment, inpatient, Epistemonikos, GRADE

Abstract

Introduction

Acute diverticulitis is one of the complications of diverticular disease. Nowadays, there is a paradigm shift regarding the use of antibiotics to manage acute uncomplicated diverticulitis in hospitalized patients, with controversial information about it.

Methods

A search was done in Epistemonikos, the most comprehensive health-related systematic review database, maintained by screening multiple information sources including MEDLINE/PubMed, EMBASE, Cochrane, among others. Data were extracted from the identified systematic reviews, data from primary studies were analyzed, which in this work considered only randomized clinical trials, a meta-analysis was done, and a summary table of results was created using GRADE methodology.

Results and Conclusions

Eleven systematic reviews were identified that included seven primary studies in total, of which two were randomized control trials. We concluded that the use of antibiotics in acute uncomplicated diverticulitis could slightly increase complications and result in a minor or no difference in the risk of recurrence and need for urgent surgery. However, the certainty of the evidence is low. Regarding hospital stay and readmission, it was not possible to evaluate the effect due to a low certainty of evidence.

Problem

Acute diverticulitis is a complication of diverticular disease in which inflammation of one or more diverticula occurs. It occurs in about 5% of individuals with diverticula¹, of which around 75% of cases correspond to acute uncomplicated diverticulitis, which refers to the presence of diverticular inflammation and the absence of complications such as intestinal perforation, abscesses, obstruction, or fistulas². The clinical condition is composed of abdominal pain, changes in bowel habits, abdominal distention, nausea, fever, and pain on palpation of the left lower quadrant³.

In cases of acute uncomplicated diverticulitis, hospital management is preferred when dealing with patients with poor oral tolerance, severe pain, comorbidities, those who are elderly, immunocompromised, or who failed with outpatient treatment². In these cases the standard treatment consists of administering antibiotics and dietary restriction, and symptom control³.

In recent years, the use of antibiotics as a cornerstone of treatment has been challenged, arguing that antibiotics would not change the clinical outcomes presented by patients. Furthermore, the fact that the antibiotics can lead to adverse effects or poor tolerance by patients must also be considered^{4,5}.

Main messages

- It is not possible to establish whether the use of antibiotics leads to increased re-admission and length of hospital stay, respectively, as the certainty of the evidence was assessed as very low.
- The use of antibiotics could make little or no difference in the risk of recurrence, complications, and the need for emergency surgery in patients with acute uncomplicated diverticulitis (low certainty of the evidence).
- No trials evaluating the effect of antibiotic use on the duration of symptoms were found.

In relation to the body of evidence to answer these questions

<p>What is the evidence? See the evidence matrix below in Epistemonikos.</p>	<p>We found 11 systematic reviews⁶⁻¹⁶ which included seven primary studies that answer the clinical question, two of them being randomized trials^{17,18}. This table and the general summary are based on the latter trials since the observational studies did not increase the certainty of the existing evidence, nor did they provide additional relevant information.</p>
<p>What type of patients were recruited in the studies? *</p>	<p>All trials included patients with acute uncomplicated diverticulitis, clinically diagnosed using computed tomography. All patients included in the trials were older than 18 years old^{17,18}. The age range in one trial was between 48 and 64 years old¹⁷, while in the other trial, the mean age of patients was 57 years old¹⁸. One trial recruited patients with a medical history of previous acute diverticulitis¹⁸.</p> <p>Patients diagnosed with or suspected of other diseases on computed tomography, such as colon cancer and inflammatory bowel disease, were excluded.</p>
<p>What types of interventions were used in the studies? *</p>	<p>In both trials, patients were managed as inpatients.</p> <p>One trial used the administration of intravenous antibiotics, amoxicillin plus clavulanic acid, for two days and then switched to an oral scheme for eight days. In allergic patients, ciprofloxacin was used in addition to metronidazole for ten days¹⁷.</p> <p>The other trial used the administration of intravenous antibiotics as intervention, cefuroxime or cefotaxime, in addition to metronidazole, carbapenems, or piperacillin-tazobactam. Then an oral scheme with ciprofloxacin or cefadroxil in addition to metronidazole. Antibiotic therapy lasted for at least seven days¹⁸.</p> <p>As a comparison, both trials used a symptomatic treatment without antibiotics, with intravenous fluids and supportive measures¹⁷ or only fluids¹⁸.</p>
<p>What kind of outcomes were measured?</p>	<p>The outcomes measured were the following:</p> <ul style="list-style-type: none"> • Readmission • Recurrence • Complications during the follow-up period • Need for emergency surgery

Methods

A search in Epistemonikos, the largest health-related systematic review database, was done by filtering multiple sources of information, including MEDLINE/PubMed, EMBASE, Cochrane, among others. For the search, the keywords were “acute diverticulitis”, “colonic diverticulitis”, “diverticular disease”, “antibiotic”, “antibacterial” and “bactericide agent”. Along with this, a search was carried out in Google Scholar to evaluate the existence of gray literature.

Data were extracted from the identified systematic reviews that answered the clinical question posed. The data from the primary studies were examined, which in this study only corresponded to randomized clinical trials since they are considered the best source of evidence, excluding observational studies.

With this information, a structured summary called FRISBEE (*Friendly Summaries of Body of Evidence using Epistemonikos*) was created, by following a pre-established format, including key messages, a summary of the body of evidence (presented as a matrix of evidence in Epistemonikos), a meta-analysis of all studies when possible, a summary table of results using the GRADE (*Grading of Recommendations Assessment, Development and Evaluation*) method, and a section on other considerations for decision-making.

- | | |
|--|--|
| | <ul style="list-style-type: none">• Length of hospital stay (days) |
|--|--|

The follow-up period in both trials was 12 months^{17,18}.

* Information on primary studies was collected from identified systematic reviews, not directly from studies unless otherwise specified.

Summary of the results

Information on the effects of antibiotic use for acute uncomplicated diverticulitis in hospitalized patients is based on two randomized trials that included 1151 patients.

In both trials, the outcomes of readmission, length of hospital stay, complications during follow-up, need for emergency surgery (1151 patients), and recurrence (1110 patients) were measured^{17,18}.

The summary of the results is as follows:

- It is not possible to clearly establish whether the use of antibiotics leads to increased readmission as the certainty of the evidence was assessed as very low.
- The use of antibiotics could make little or no difference in the risk of recurrence of acute diverticulitis (low certainty of the evidence).
- The use of antibiotics makes little or no difference in the risk of developing complications during the follow-up of patients with acute uncomplicated diverticulitis (low certainty of the evidence).
- The use of antibiotics could make little or no difference in the risk of needing emergency surgery in patients with acute uncomplicated diverticulitis (low certainty of the evidence).
- It is not possible to clearly establish whether the use of antibiotics decreases the duration of the hospital stay since the certainty of the evidence was evaluated as very low.
- No trials evaluating the duration of symptoms were found.

Antibiotics for acute uncomplicated diverticulitis in hospitalized patients				
Patients	Hospitalized patients with acute uncomplicated diverticulitis			
Intervention	Antibiotics			
Comparison	Support handling			
Outcomes	Absolute effect*		Relative effect (95% CI)	Certainty of evidence (GRADE)
	WITHOUT antibiotics	WITH antibiotics		
	Difference: patients per 1000			
Readmission*	140 per 1000	197 per 1000	RR 1.41 (0.77 to 2.57)	⊕○○○ ^{1,2,3} Very low
	Difference: 57 more (patients) (32 less to 219 more)			
Recurrence**	97 per 1000	101 per 1000	RR 1.04 (0.74 to 1.48)	⊕⊕○○ ^{1,2} Low
	Difference: 4 more (patients) (25 less to 46 more)			
Complications during follow-up (12m)***	17 per 1000	28 per 1000	RR 1.62 (0.74 to 3.54)	⊕⊕○○ ^{1,2} Low
	Difference: 11 more (patients) (4 less to 44 more)			
Emergency surgery	10 per 1000	5 per 1000	RR 0.52 (0.13 a to 2.10)	⊕⊕○○ ^{1,2} Low
	Difference: 5 more (patients) (9 less to 11 more)			
Hospital stay	2 days	1.59 days	--	⊕○○○ ^{1,2,3} Very low
	MD: 0.41 days less (Range of error: 1.2 less to 0.37 more)			
Duration of symptoms	The outcome was not measured or reported.		--	--

Margin of error: 95% confidence Interval (95% IC).
RR: Relative Risk.
MD: Mean difference.
GRADE: Grades of Evidence of the GRADE Working Group (see below).

*Risk/average WITHOUT antibiotics are based on the risk/average of the control group in the studies. Risk/average WITH antibiotics (and its margin of error) is calculated from the relative effect/ mean difference (and its margin of error).

* Readmission corresponds to hospital readmission within one month after discharge due to persistent symptoms, with or without complications.
** Recurrence refers to a new episode of acute diverticulitis that occurred at least one month after discharge.
*** Complications include colonic perforation, intraperitoneal abscess, intestinal obstruction, intestinal bleeding, and colovesical fistula.

¹ The level of certainty of the evidence was lowered due to the risk of bias since the evaluated studies show selection bias, detection bias, and reporting bias.
² The level of certainty of the evidence was lowered due to inaccuracy since when each extreme of the result of the relative effect is evaluated, different clinical behaviors are promoted to be taken.
³ The level of certainty of the evidence was lowered due to inconsistency because heterogeneity is found between the evaluated studies, expressed by an index I² > 70%.

Follow the link to access the interactive version of this table ([Interactive Summary of Findings - iSoE](#))

In relation to the certainty of evidence (GRADE)*

⊕⊕⊕⊕

High: The research provides a very good indication of the likely effect. The probability that the effect is substantially different † is low.

⊕⊕⊕○

Moderate: The research provides a good indication of the likely effect. The probability that the effect is substantially different † is moderate.

⊕⊕○○

Low: The research provides some indication of the likely effect. However, the probability that the effect is substantially different † is high.

⊕○○○

Very low: The research does not provide a reliable estimate of the likely effect. The probability that the effect is substantially different † is very high.

*This is also called 'quality of evidence' or 'confidence in estimates of effect'.

†Substantially different = a difference large enough to affect the decision.

Other considerations for decision making

Whom does this evidence apply to?

The results of this study apply to patients with acute uncomplicated diverticulitis who are treated in an in-hospital setting.

These results could be extrapolated to immunocompetent adult patients, with no decompensated comorbidities and with no signs of sepsis.

This evidence does not apply to pregnant or lactating patients.

In relation to the outcomes included in this summary

The outcomes selected in the table summarizing the results are those considered critical for clinical decision making, according to the opinions of the authors, which are in agreement with those results reported by the systematic reviews.

According to the authors, the outcome regarding "duration of symptoms" was considered relevant for decision-making; however, it was not reported in the systematic reviews evaluated.

Harm/benefit balance and certainty of the evidence

The body of evidence shows no benefit from adding antibiotics for the outcomes of recurrence, complications, and the need for emergency surgery; however, the certainty of the evidence was assessed as low.

In the case of the outcomes of readmission and hospital stay, it is not possible to conclude the harm or benefit of the intervention since the certainty of the evidence was assessed as very low.

Although the evidence presented does not show a benefit from antibiotics, it is not possible to make an adequate balance between risks and benefits due to the uncertainty of their effects, which is associated with the limitations of the existing evidence.

Resource considerations

In some systematic reviews analyzed in this summary, it is mentioned that if patients are not treated with antibiotics, this could reduce costs associated with the care of these patients⁸.

It is also noted that in those patients in whom the clinician decides to administer antibiotics, their oral administration could also reduce hospitalization costs⁷.

However, considering the low certainty of the evidence, it is not possible to make an adequate balance between costs and benefits.

What do patients and their caregivers think?

Although antibiotic treatment for this pathology is common practice, non-pharmacological management could be a feasible and safe option in a subgroup of stable patients without comorbidities.

Keeping patients under observation without drug therapy would avoid the possibility of possible adverse reactions to the antibiotic, in addition to reducing bacterial resistance to the drug.

Differences between this summary and other sources

The NICE (National Institute for Health and Care Excellence) clinical guidelines (2019) suggest considering symptomatic management with simple analgesia in patients with acute uncomplicated diverticulitis who are systemically well. On the other hand, the National Institute for Health and Care Excellence clinical guidelines recommend using antibiotics for those patients who are systemically not well (but who do not meet the criteria for acute complicated diverticulitis), with significant comorbidities or immunocompromised patients¹⁹.

The American Society of Colon and Rectal Surgeons (ASCRS) guidelines (2020) mention that a select group of patients with acute uncomplicated diverticulitis can be treated without antibiotics, including healthy patients, without comorbidities, with early stages of development of the condition⁴.

The European Society of Coloproctology Guidelines (2020) indicates that patients with acute uncomplicated diverticulitis do not require antibiotics on a routine basis, and that antibiotics should be saved only for immunocompromised patients or those with sepsis⁵.

The World Society of Emergency Surgery (WSES) guidelines (2020) report that antibiotics may not be necessary for the treatment of acute uncomplicated diverticulitis²⁰.

Could this information change in the future?

The information provided in this evidence summary is likely to change over time for the outcomes of recurrence, complications, and emergency surgery since the certainty of the evidence is low. In the case of readmission and hospital stay, the information is very likely to change since the certainty of the evidence is very low.

A trial was found²¹ that was not included in any systematic review included in this study that concludes that the administration of antibiotics does not reduce the hospital stay in patients with acute uncomplicated diverticulitis.

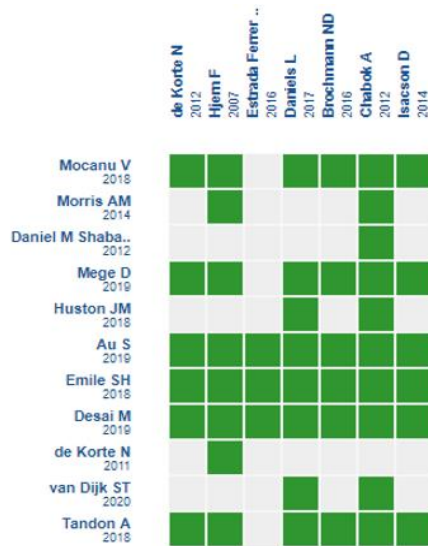
Two ongoing systematic reviews were identified in the PROSPERO (International Prospective Register of Systematic Reviews) search^{22,23}.

No ongoing trials were identified in the World Health Organization International Clinical Trials Registry Platform.

It should be noted that the authors of this summary believe that it would be very interesting to study this same clinical question in a primary care setting.

How did we do this summary?

Using automated and collaborative methods, we collected all the relevant evidence for the question of interest which was presented in an evidence matrix.



An evidence matrix is a table that compares systematic reviews that answer the same question. Rows represent systematic reviews, and columns show primary studies. The boxes in green correspond to studies included in the respective revisions. The system automatically detects new systematic reviews including any of the primary studies in the matrix, which will be added if they actually answer the same question.

Please, follow the link to access the **interactive version**: [Antibióticos versus manejo sintomático para el tratamiento de diverticulitis aguda no complicada en pacientes hospitalizados.](#)

Contribution roles

CAQ: conceptualization, methodology, software, validation, formal analysis, research, resources, data management, manuscript, manuscript revision, visualization, project administration and acquisition of funds. LTB: conceptualization, methodology, validation, formal analysis, research, resources, data management, manuscript, visualization, project administration and acquisition of funds. GGB: conceptualization, methodology, validation, formal analysis, research, resources, data management, manuscript, visualization and acquisition of funds. AZC: conceptualization, validation, manuscript revision, visualization, monitoring, project administration and acquisition of funds.

Acknowledgments

We would like to thank doctors Francisca Verdugo and Camila Avila for introducing and instructing the work team in the FRISBEE method

Notes

If new systematic reviews on this topic are published after the publication of this summary, a notice of “new evidence” will be displayed at the top of the matrix. Although the project contemplates the periodic updating of these summaries, users are invited to comment on the Medwave website or contact the authors by email if they believe that there is evidence that motivates an earlier update.

After creating an account on Epistemonikos, when saving the matrices, you will receive automatic notifications every time there is new evidence that may potentially answer this question.

This paper is part of the Epistemonikos Evidence Synthesis Project. It is prepared with a pre-established methodology, following rigorous methodological standards and an internal peer review process. Each of these papers corresponds to a summary, called FRISBEE (*Friendly Summary of Body of Evidence using Epistemonikos*), whose main objective is to synthesize the set of evidence of a specific question in a friendly format for clinical professionals. Its main resources are based on the Epistemonikos evidence matrix and the analysis of results using the GRADE methodology. Further details of the methods to make this FRISBEE are described here: (<http://dx.doi.org/10.5867/medwave.2014.06.5997>)

The Epistemonikos Foundation is an organization that seeks to bring information to those who make decisions in health through the use of technologies. Its main development is the Epistemonikos database.

(www.epistemonikos.org).

Competing interests

The authors declare that they have no conflicts of interest with the subject of this manuscript.

Ethical statement

Given that this research is a study on secondary sources of information, it does not need approval by an ethics committee.

Funding

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Data repository declaration

The data are available upon request and evaluation of the rationale by the authors.

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