ORIGINAL PAPER

Non-antibiotic treatment of uncomplicated acute diverticulitis is applicable and safe in our environment. A prospective multicenter study

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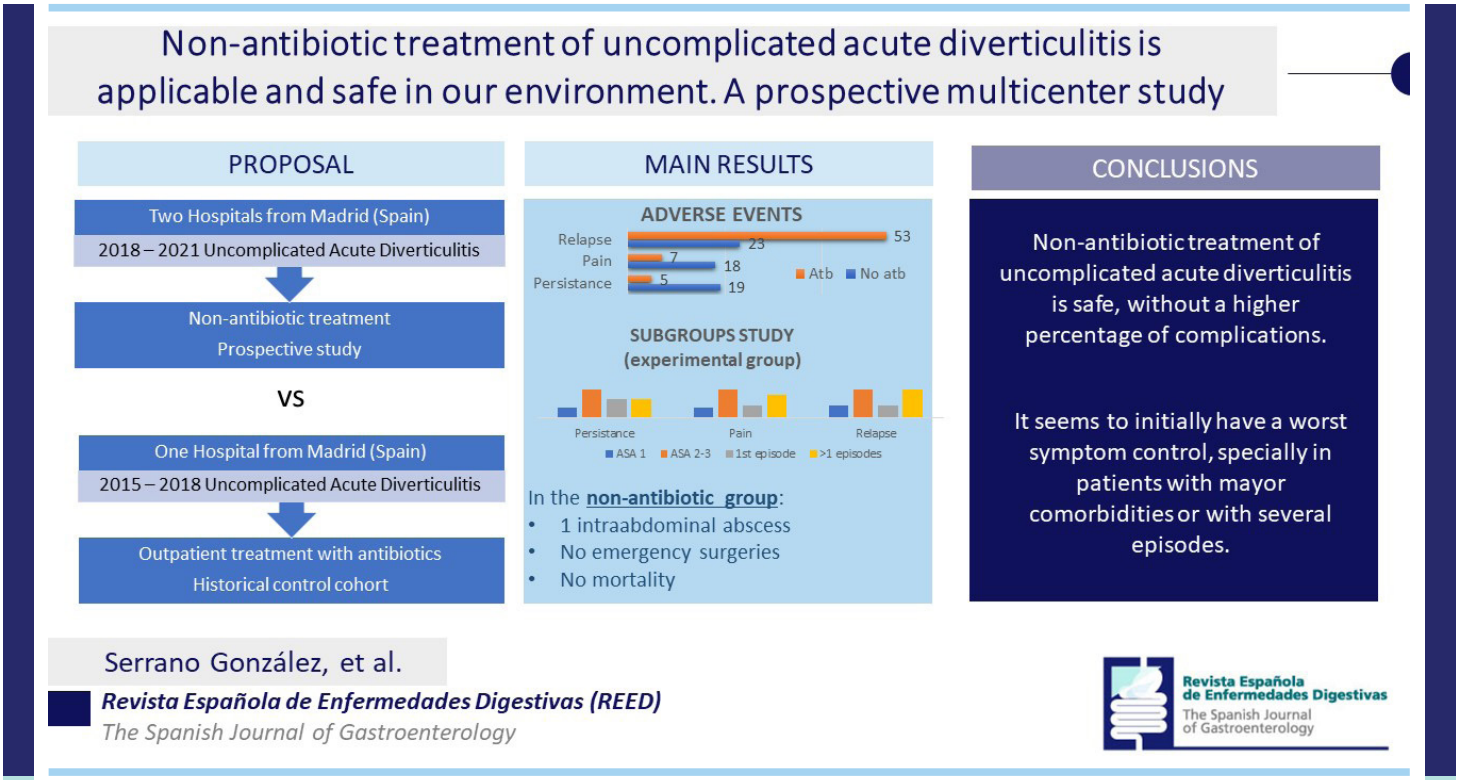

Lay summary

Background: a diverticulum is a pouch-like structure that appears in both the small and large intestine, being more common in the latter. Up to 70 % of people over 70 years old have them. Acute diverticulitis is the inflammation of these diverticula, developing abdominal pain with or without fever. In mild cases, treatment consisted of digestive rest, pain killers and antibiotics. However, the possibility of treating these cases without antibiotics has been studied in the past few years.
Objective: to present the results of non-antibiotic treatment after starting this protocol in two hospitals in Madrid, and to assess its safety and effectiveness.
Method: two groups were created: a current group of patients treated with diet and analgesics, and a control group with patients treated in the past with diet, analgesics and antibiotics. The results from both groups were compared.
Results: in the study group, only one of the 182 patients developed a complication of the inflamed diverticula, and no patients died. Reappearance of the disease in long-term follow-up was more frequent in the group treated with antibiotics than in the current group. However, symptoms disappeared faster in patients treated with antibiotics.
Conclusions: to remove antibiotics from the treatment of acute diverticulitis does not imply a worse outcome. However, total recovery might take longer.

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ABSTRACT

Introduction: acute diverticulitis is one of the most frequent underlying causes behind individuals attending the Emergency Room with abdominal pain. The most widespread therapy for acute uncomplicated diverticulitis includes outpatient treatment with antibiotics; however, several publications indicate that patients can also be successfully treated without antibiotics. The results of the implementation of this more recent protocol in two hospitals in Madrid are presented.

Methods: an observational prospective study was performed. Participants were patients diagnosed with uncomplicated acute diverticulitis at two hospitals in Madrid, Hospital Universitario de Torrejón and Hospital Universitario Puerta de Hierro Majadahonda, between December 2018 and August 2021, treated on an outpatient basis without antibiotic therapy. The study group was compared with a control group, composed of patients diagnosed with uncomplicated acute diverticulitis and treated with outpatient antibiotic therapy at Hospital Universitario Puerta de Hierro between March 2015 and March 2018.

Results: three hundred and sixty-one patients were included, 182 in the study group and 179 in the control group. Diverticulitis was persistent in 19 patients (10.4 %) in the study group, who were not treated with antibiotics, and in five patients (2.8 %) in the control group, treated with outpatient antibiotic therapy ($p = 0.004$). Recurrences occurred in 23 patients (12.6 %) in the study group, and in 53 patients (29.6 %) in the control group ($p < 0.0001$). The analysis of the complications found no significant differences between both groups ($p = 0.109$). No urgent surgical intervention or mortality was recorded in the study group.

Conclusions: in our environment, symptomatic non-antibiotic treatment of uncomplicated acute diverticulitis cases is safe, without showing a higher rate of complications. Although, there seems to be a worse initial symptom control.

Keywords: Diverticulitis. Anti-bacterial agents. Outpatients. Analgesia. Anti-inflammatory agents. Non-steroidal. Humans.

INTRODUCTION

Diverticular disease (DD) is one of the most common abdominal pathologies. The prevalence has increased in the past few decades. About 20 % of the population over 40 years old is considered to have this condition, and this rate increases to 60 % at the age of 60 and up to 75 % of the population over 80 years (1,2). Clinical presentation happens in 1-4 % of patients (3,4) and recurrences occur in around 15-30 % of patients (5).

Uncomplicated acute diverticulitis (UAD) is defined as a case of lower abdominal pain with diverticular inflammation, associated or not with altered pericolic fat. It also includes an altered blood analysis, and is diagnosed using imaging tests (6).

Two classifications are most commonly used: the Hinchey classification (7) and the World Society of Emergency Surgery (WSES) classification (8). Modified Hinchey's classification uses radiologic findings to divide cases of acute diverticulitis (AD):

- 0: mild AD.
- Ia: pericolic inflammation.
- Ib: pericolic abscess.
- II: distant abscess.
- III: purulent peritonitis.
- IV: fecaloid peritonitis.

WSES classification divides cases of AD as:

- UAD: thickening of the colonic wall and increased density of the pericolic fat.
- Complicated AD:
  - 1A: pericolic air bubbles of pneumoperitoneum or little pericolic fluid without abscess.
  - 1B: abscess ≤ 4 cm.
  - 2A: abscess > 4 cm.
  - 2B: distant pneumoperitoneum.
  - 3: diffuse fluid without distant free air.
  - 4: diffuse fluid with pneumoperitoneum.

If we look at the Modified Hinchey Classification, UAD includes stages 0 and Ia (7), and the "uncomplicated" degree is in the WSES classification. Patients presenting obstruction, hemorrhage, intraabdominal abscesses, fistulae or intestinal perforation, as well as presence of air bubbles, are excluded.

In the past couple of decades, treatment of this pathology has become more conservative. Outpatient treatment protocols are considered to be safe and effective in mild forms. Therefore, this is the standard in most hospitals in Spain. Also, management of severe cases has changed, with stricter indications for surgery and less aggressive approaches (laparoscopy, lavage and drainage, resection and primary anastomosis, etc.) (9-13).

Conflict of interest: the authors declare no conflict of interest.

Author contributions: Javier Serrano González: research conception, writing of the manuscript. Laura Román García de León: research development, review and editing of the manuscript. Pablo Galindo Jara: data conservation, review of the manuscript. José Luis Lucena de la Poza: research conception, review of the manuscript. Arsenio Sánchez Movilla: research conception, review of the manuscript. Laura Colao García: research development, review of the manuscript. Jesús Gabriel García Schiever: review and editing of the manuscript. David Varillas Delgado: methodology and formal analysis.

Artificial intelligence: the authors declare that they did not use artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

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The Swedish study AVOD (2012) analyzed the possibility of managing patients with UAD without risk factors avoiding the use of antibiotics (14). Several trials and meta-analyses have been subsequently published, showing good results (15-20). In addition, a recent Cochrane review concluded that the benefits of therapy with antibiotics are uncertain (21). However, the use of antibiotics to treat these mild cases is the most common treatment strategy in our environment. Here, we present a study conducted in two hospitals in Madrid (Spain) implementing a new treatment protocol for patients with UAD without using antibiotics.

MATERIAL AND METHODS

Study design

A prospective observational comparative study was performed with a historical cohort. Participants were patients with UAD treated on an outpatient basis without antibiotics. They were selected from Hospital Universitario de Torrejón (HUT) and Hospital Universitario Puerta de Hierro Majadahonda (HUPHM) between December 2018 and August 2021. This study was approved by the Ethics Committee of the Autonomous Community of Madrid on June 10, 2019 (certificate 6/19).

The historical control cohort was comprised of patients diagnosed with UAD treated as outpatients at the HUPHM between March 2015 and March 2018. Management included oral antibiotics: amoxicillin/clavulanic acid 875/125 mg every eight hours or ciprofloxacin 500 mg/12 hours associated with metronidazole 500 mg/8 hours if the patient was allergic to penicillin. Treatment lasted seven days, and included analgesics and diet recommendations. Follow-up of outpatients at the Colorectal Unit was conducted, and the first visit was five to ten days after diagnosis.

Study group

Patients diagnosed by the Emergency Service team and treated by the General Surgery Service team from both hospitals, HUT and HUPHM, were included via consecutive sampling. Patients included in the study were informed of the therapeutic protocol they were going to follow and the study they were part of, and they gave their consent to participate. The study inclusion criteria were:

- Diagnosed of UAD:
  - Compatible clinical presentation, laboratory results and computed tomography (CT) scan.
    - Body temperature ≤ 38 °C.
    - White cell count ≤ 15,000/µl.
    - High-sensitivity C-reactive protein (CRP) ≤ 15mg/dl.
    - CT scan compatible with UAD.
- Age between 18 and 70 years.
- ASA I-III.
- Sufficient social and/or family support.
- Patient able to ingest food orally.

Exclusion criteria:
- Complicated AD (evidence of stenosis, abscess, pneumoperitoneum or fistula in the CT scan, or signs of hemorrhage, obstruction or sepsis).
- Pregnant patients.
- Immunosuppressed patients (cancer, chronic corticoid treatment, treatment with other immunosuppressors, chronic kidney failure).
- Body mass index (BMI) ≥ 40 kg/m^2.
- Use of antibiotics at the ER or the week prior for any other reason.

Objectives

The main objective of this study was to analyze the cases of UAD with poor evolution when treated without antibiotics in the participating hospitals, and compare them with those of the historical control group (CG) to confirm if the treatment is valid. The definition of poor evolution includes persistent cases (abdominal pain, with or without fever, reappearing in the first 30 days), relapses (new episode after 30 days) or complications (any other outcome than total recovery) (14). Residual pain was also included in the study of adverse events as a complication.

The secondary objective was to study the clinical and demographic characteristics of the study group (SG) that could be considered as risk factors (RF) of poor evolution with the experimental treatment.

Studied variables

Collected data included demographic variables (age, gender, American Society of Anesthesiologists [ASA] classification), clinical variables (history of AD, duration of symptoms, body temperature, analytical results) and end results (persistent cases, relapses or complications).

Statistical analysis

Numerical variables are described with median and percentiles, and qualitative variables using frequencies and percentages. Since variables do not follow a normal distribution, the comparison between cohorts was made using the non-parametric Mann-Whitney U test. For qualitative variables, a contingency table using the Chi-squared test was used. Results with $p < 0.05$ indicate statistical significance between both groups. All our data were analyzed using the SPSS® software package version 21.0 (SPSS, Chicago, Illinois, United States).

Management protocol

- The patient is discharged/outpatient treatment.
- Pain control: acetaminophen 1 g every eight hours, alternating with metamizole 575 mg every eight hours.
- Clear liquid diet for the first 48 hours, followed by a progressive low fiber diet (informative brochures are given to the patients explaining what food is permitted).
- Reevaluation seven to ten days later at the Colorectal Unit with a new blood analysis.
- Telephone follow-up interview after one month.
- Outpatient follow-up, either in person or via telephone.

RESULTS

Through December 2018 to August 2021, 195 patients were diagnosed with UAD (100 at HUT, 95 at HUPHM). Thirteen patients were excluded: three received antibiotics at the Emergency Room, one was being treated with antibiotics for other reasons the week before, three were starting antibiotic treatment prescribed by their family doctor (without clinical worsening) and six due to lack of follow-up. The SG included 182 patients (96 from the HUT and 86 from the HUPHM); meanwhile, the CG included 179 patients. Minimum follow-up time was six months (Fig. 1).

Statistical differences were found between both groups regarding age and CRP, none of them were clinically relevant (Table 1).

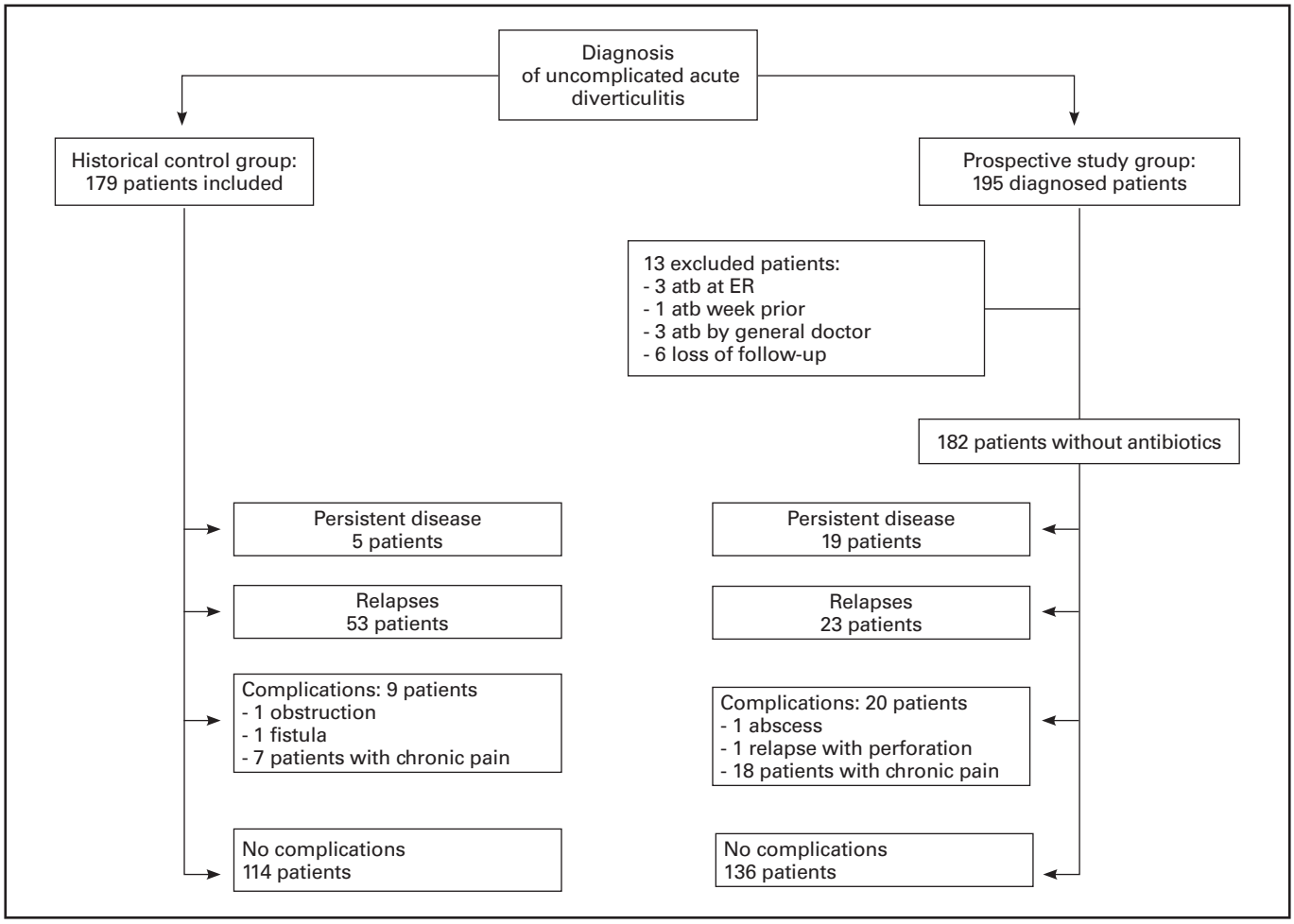

Fig. 1. Flow chart of patients. atb: antibiotic treatment; ER: Emergency Room.

Table 1. *Demographics and patients' characteristics*

	Non-antibiotic treatment (n = 182)	Antibiotic treatment (n = 179)	*p*-value
Age (years)/mean (SD)	55.6 (12)	51.9 (9.4)	*0.001*
Gender (%M : %F)	46 : 54	55 : 45	0.082
ASA (%I : %II : %III)	36 : 56 : 7	33 : 62 : 5	0.4
Evolution time (days)/median (p25; p75)	2 (1; 3)	2 (1; 3)	0.194
Body temperature (°C)/median (p25; p75)	36.3 (36; 36.9)	36 (36; 36.6)	0.073
CRP (mg/dl)/median (p25; p75)	5.1 (2.1; 8.4)	5.8 (3.4; 10.5)	*0.005*
White cell count (µl)/median (p25; p75)	11,185 (9,030; 13,235)	11,360 (8,770; 13,600)	0.482
Neutrophil to lymphocyte ratio/median (p25; p75)	4 (2.7; 5.4)	3.9 (2.7; 6.2)	0.400

ASA: American Society of Anesthesiologists; CRP: C-reactive protein; SD: standard deviation.

Main objective

Nineteen patients with persistent disease were recorded in the SG (10.4 %) treated without antibiotics, and five patients in the CG (2.8 %) treated with antibiotics (p = 0.004). Relapses appeared in 23 patients of the SG (12.6 %) and in 53 patients of the CG (29.6 %) (p < 0.0001). Adverse events in the SG were one case (0.6 %) of an intraabdominal abscess that did not require percutaneous drainage (Clavien-Dindo II), one case (0.6 %) of relapse with a diagnosis of complicated AD with colonic perforation (Clavien-Dindo IIIb), and 18 patients (9.9 %) with chronic pain after complete recovery of the acute episode (Clavien-Dindo I). In the CG, these events were one patient (0.6 %) with AD associated with intestinal obstruction and one patient (0.6 %) with a fistula (both Clavien-Dindo IIIb, requiring urgent surgery) and seven patients (3.9 %) with residual pain (Clavien-Dindo I). Study of the complications did not show significant differences between both groups (p = 0.109) (Fig. 2).

Maximum follow-up time in the SG was 24 months, while follow-up of some patients in the CG was up to 50 months. To avoid a selection bias due to a loss of follow-up, a Kaplan-Meier survival curve (Fig. 3) analysis was used to stratify relapses according to the time passed since the initial episode of AD. This analysis showed that the differences between both groups were more noticeable as the follow-up time increased; relapse percentages in patients with 6-12 months follow-up were 9.3 % SG *vs* 15.5 % CG (p = 0.086) and in patients with 12-24 months follow up were 12.1 % SG *vs* 25.9 % CG (p < 0.001). There were five cases of right AD, with just one relapse, no persistent disease and no chronic pain.

To avoid selection biases when analyzing the results, given the theoretical worse evolution of inflammatory and infectious diseases in patients with more comorbidities, and the well-known higher risk for a relapse in those with previous episodes of AD, subgroups were analyzed according to the medical record of the patients (ASA classification) and previous diagnosis of AD. Parameters of poor evolution in both branches were compared and the results are shown in table 2.

Of the 19 patients of the SG with persistent symptoms, five (2.8 %) were admitted to hospital for intravenous antibiotics after returning to the Emergency Room; only one (0.5 %) due to an intraabdominal abscess and the rest for showing clinical deterioration without worsening on the CT scan. Oral antibiotics were used in seven patients (3.8 %) that returned to the ER but did not require hospital admission. Another seven patients (3.8 %) showed persistent symptoms during follow-up at the Colorectal Unit, all of which improved without any other treatment.

No emergency surgery was performed due to AD. In the SG, two subsequent surgeries were documented, one due to a relapse with complicated acute diverticulitis with associated perforation, and another due to iatrogenic perforation during a colonoscopy performed two months after the original episode. In the CG, seven patients underwent surgery after several episodes of AD; one case of obstruc-

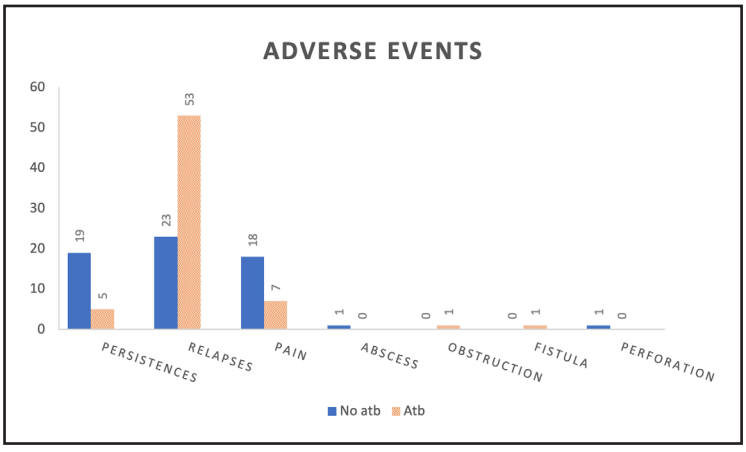

Fig. 2. *Adverse events in the study groups. atb: antibiotic treatment.*

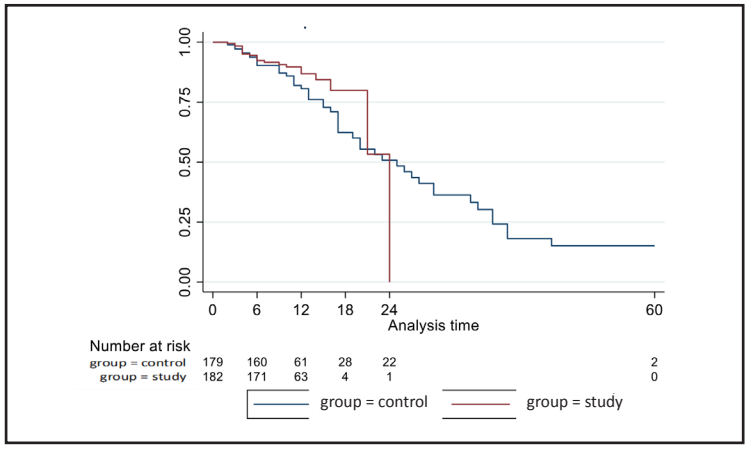

Fig. 3. *Kaplan-Meier curve, relapses.*

tion with diagnostic uncertainty, one who developed colon cancer four years after the episode of UAD and one after developing a colovesical fistula.

As a complementary analysis, those patients from the SG who suffered a relapse during the study period, managed without antibiotics and with a follow-up of over six months were studied. This group consisted of 17 patients. Amongst these, two patients (11.8 %) had persistent disease, compared with 17 (10.3 %) of those that were treated only once (p = 0.85). Three patients (17.7 %) had a relapse, compared with 20 (12.1 %) of the patients treated only once with this protocol (p = 0.51). No significant differences were found when analyzing the presence of chronic pain; two cases (11.8 %) *vs* 20 (12.1 %) of the total of the SG (p = 0.97).

Secondary objective

In order to identify RF for adverse evolution, the patient's clinical and demographic characteristics were analyzed and correlated with the development of adverse events. The results are shown in table 3.

Table 2. *Subgroups study*

	ASA 1			ASA 2-3		
	Control group	Experimental group	*p*	Control group	Experimental group	*p*
Persistence	2 (3.4 %)	5 (7.6 %)	0.31	3 (2.5 %)	14 (12.1 %)	*0.004*
Relapses	4 (6.8 %)	6 (9.1 %)	0.634	49 (40.8 %)	17 (14.7 %)	*< 0.001*
Adverse events	3 (5.1 %)	5 (9.1 %)	0.387	6 (5 %)	15 (13.8 %)	*0.02*
	1st episode			> 1 episodes		
	Control group	Experimental group	*p*	Control group	Experiment group	*p*
Persistence	4 (3.6 %)	9 (10 %)	0.07	1 (1.5 %)	9 (10 %)	*0.03*
Relapses	27 (24.6 %)	6 (6.7 %)	*0.001*	26 (37.7 %)	17 (18.9 %)	*0.008*
Residual pain	3 (2.7 %)	6 (6.7 %)	0.175	4 (5.8 %)	11 (12.4 %)	0.163

ASA: American Society of Anesthesiologists.

Table 3. *Correlation between adverse events and patients' characteristics*

	Relapses			Persistent disease			Pain		
	No	Yes	*p*	No	Yes	*p*	No	Yes	*p*
Age (years)/median (SD)	53.88 (11.2)	53.55 (9.7)	*0.579*	54.12 (10.9)	49.54 (11.1)	*0.055*	53.94 (10.7)	52.72 (13.7)	*0.512*
Gender (%M : %W)	53.7 : 46.3	39.5 : 60.5	*0.028*	51.6 : 48.4	37.5 : 62.5	*0.181*	51.5 : 48.5	36:64	*0.135*
ASA (%1 : %2-3)	40.4 : 59.6	13.2 : 86.8	*< 0.001*	35 : 65	29.2 : 70.8	*0.561*	34.7 : 65.3	32:68	*0.782*
Episode number (%1st : % > 1)	59:41	43.4 : 56.6	*0.015*	55.7 : 44.3	56.5 : 43.5	*0.935*	57.1 : 42.9	37.5 : 62.5	*0.062*
Second treatment w/o antibiotics/cases (%)	20 (87 %)	3 (13 %)	*0.051*	17 (89.5 %)	2 (10.5 %)	*0.851*	16 (88.9 %)	2 (11.1 %)	*0.799*
Evolution time (days)/median (p25; p75)	2 (1; 3)	2 (1; 3)	*0.7*	2 (1; 3)	2.5 (1; 3.5)	*0.407*	2 (1; 3)	2 (1; 3)	*0.958*
CRP (ml)/median (p25; p75)	5.5 (2.7; 9.3)	5.6 (3.1; 10.7)	*0.37*	5.6 (3; 9.4)	2.8 (0.8; 9.4)	*0.051*	5.7 (3; 9.5)	3 (1.2; 6.9)	*0.018*
White cell count (µl)/median (p25; p75)	11,270 (9,260; 13,570)	10,935 (8,245; 12,150)	*0.085*	11,180 (9,070; 13,390)	11,810 (8,310; 14,180)	*0.979*	11,080 (8,770; 13,390)	12,600 (10,910; 16,000)	*0.024*
Neutrophil lymphocyte ratio/median (p25; p75)	3.9 (2.7; 5.9)	3.9 (2.5; 5.6)	*0.786*	4.1 (2.8; 5.7)	3.3 (2.1; 5.7)	*0.086*	3.9 (2.7; 5.7)	4.2 (3; 5.7)	*0.675*

ASA: American Society of Anesthesiologists.

DISCUSSION

Despite the high prevalence of DD and its complications, its origin and treatment are still generating debate. Based on actual physiopathological theories (altered intraluminal pressure, genetic factors, obesity, etc.) (22), the systematic use of antibiotics to treat UAD does not add extra benefits in recovery or the development of complications. Recurrences, which appear in 15 to 30 % of cases (23), have not diminished in the last few decades, despite recent changes in management. Most recent editions of management guides for DD do not recommend a systematic use of antibiotics to treat uncomplicated cases in low-risk patients (24-27). Recommended treatment is based on analgesia and intestinal rest.

The AVOD study (14) was the first randomized clinical trial to test a non-antibiotic treatment in UAD. It concluded that antibiotics do not speed up recovery, nor prevent relapses or complications. Also, the DIVER study (11) proved that outpatient treatment of UAD cases with an outpatient follow-up was safe and effective. In 2021, the DINAMO study (19) combined these concepts, offering data that showed a non-inferiority of outpatient non-antibiotic treatment when compared with antibiotics. However, although we have all this information, and the meta-analyses (18) that support it, the use of antibiotics is the most common treatment in our society. Limiting its systematic use can bring positive effects both individually (less adverse reactions such as pseudomembranous colitis, diarrhea, candidiasis, etc.) and collectively (decrease of bacterial resistances).

In our series, persistent symptoms and the development of chronic pain (most prevalent complication) was more prevalent in the group treated without antibiotics (SG). This poorer development was also more frequent in the subgroups with a theoretical initial higher risk (those with more comorbidities and a personal history of previous episodes of AD). It is possible that these poorer results might be the consequence of the anti-inflammatory effects of some antibiotics (this effect is known when macrolides are used in some situations), which we are not providing to our patients in this protocol.

Relapses were more frequent in the group treated with antibiotics (CG). This statistic, when globally analyzing the whole population of our study, could be related to a follow-up bias. The Kaplan-Meier curve shows that the longer the follow-up is, the higher the percentage of relapses and the greater the differences are between both groups.

Only one important adverse event was reported in the SG; an abscess appeared after the diagnosis of UAD. Treatment consisted of intravenous antibiotics, without requiring any invasive treatment. No emergency surgical treatment or mortality were reported. Management without antibiotics of a second episode of UAD does not have a worse outcome compared to patients treated only once. Thus, we believe that this reflects the security of this protocol.

In our search for risk factors of poor evolution, our data could help select patients to obtain better results. When analyzing the development of relapses, female gender, existing previous comorbidities and a personal history of previous symptomatic AD episodes have been shown to be important factors. However, none of them showed a significant statistical difference when chronic pain or persistent disease were analyzed. We believe, without real clinical relevance, our results support that a higher white blood cell count could predict the development of residual pain, and that a lower concentration of CRP could be related with persistent symptoms and long-term pain. We consider that this aspect requires validation to correlate it with clinical practice.

Regarding weak points of the study, we highlight that the historical character of the control group has not allowed a more exact comparison between both groups in our study. Follow-up bias between both groups increased the number of relapses in the control cohort. Study of the causes of relapsing cases and residual chronic pain control observed in the SG could be a focus for future research.

CONCLUSIONS

In our environment, non-antibiotic outpatient treatment of cases of UAD in patients without risk factors of poor evolution is safe, and does not carry higher rates of complications or invasive procedures (percutaneous drainage or surgical procedure). Although it seems to report poorer initial symptom control, there are less relapses than in patients treated with antibiotics. These results are more evident in patients with more comorbidities and in those with a personal history of AD. Further studies are necessary to confirm these results.

Key points

- Non-antibiotic treatment in patients with UAD and no risk factors are possible. Nevertheless, it is not common practice in our environment.
- With a proper patient selection, outpatient management without antibiotics is safe and effective.
- This protocol could be considered by other hospitals to modify the classical treatment of this disease.

REFERENCES

1. Peery AF, Barrett PR, Park D, et al. A high-fiber diet does not protect against asymptomatic diverticulosis. Gastroenterology 2012;142(2):266-72.e1. DOI: 10.1053/j.gastro.2011.10.035
2. Peery AF, Keku TO, Martin CF, et al. Distribution and characteristics of colonic diverticula in a United States screening population. Clin Gastroenterol Hepatol 2016;14(7):980-5.e1. DOI: 10.1016/j.cgh.2016.01.020
3. Everhart JE, Ruhl CE. Burden of digestive diseases in the United States part II: lower gastrointestinal diseases. Gastroenterology 2009;136(3):741-54. DOI: 10.1053/j.gastro.2009.01.015
4. Shahedi K, Fuller G, Bolus R, et al. Long-term risk of acute diverticulitis among patients with incidental diverticulosis found during colonoscopy. Clin Gastroenterol Hepatol 2013;11(12):1609-13. DOI: 10.1016/j.cgh.2013.06.020
5. Broderick-Villa G. Hospitalization for acute diverticulitis does not mandate routine elective colectomy. Arch Surg 2005;140(6):576. DOI: 10.1001/archsurg.140.6.576
6. Tursi A, Papa A, Danese S. Review article: the pathophysiology and medical management of diverticulosis and diverticular disease of the colon. Aliment Pharmacol Ther 2015;42(6):664-84. DOI: 10.1111/apt.13322
7. Kaiser AM, Jiang JK, Lake JP, et al. The management of complicated diverticulitis and the role of computed tomography. Am J Gastroenterol 2005;100(4):910-7. DOI: 10.1111/j.1572-0241.2005.41154.x
8. Sartelli M, Moore FA, Ansaloni L, et al. A proposal for a CT driven classification of left colon acute diverticulitis. World J Emerg Surg 2015;10(1):3.
9. Morris AM, Regenbogen SE, Hardiman KM, et al. Sigmoid diverticulitis. JAMA 2014;311(3):287. DOI: 10.1001/jama.2013.282025
10. Regenbogen SE, Hardiman KM, Hendren S, et al. Surgery for diverticulitis in the 21st century. JAMA Surg 2014;149(3):292. DOI: 10.1001/jamasurg.2013.5477
11. Biondo S, Golda T, Kreisler E, et al. Outpatient versus hospitalization management for uncomplicated diverticulitis. Ann Surg 2014;259(1):38-44. DOI: 10.1097/SLA.0b013e3182965a11
12. Reyes-Espejel L, Ruiz-Campos M, Correa-Rovelo JM, et al. Sigmoidectomy with primary anastomosis for complicated diverticulitis. Rev Gastroenterol Mex 2015;80(4):255-9. DOI: 10.1016/j.rgmxen.2015.07.007

13. Chabok A, Thorisson A, Nikberg M, et al. Changing paradigms in the management of acute uncomplicated diverticulitis. Scand J Surg 2021;110(2):180-6. DOI: 10.1177/14574969211011032

14. Chabok A, Påhlman L, Hjern F, et al. Randomized clinical trial of antibiotics in acute uncomplicated diverticulitis. Br J Surg 2012;99(4):532-9. DOI: 10.1002/bjs.8688

15. Mege D, Yeo H. Meta-analyses of current strategies to treat uncomplicated diverticulitis. Dis Colon Rectum 2019;62(3):371-8. DOI: 10.1097/DCR.0000000000001295

16. Au S, Aly EH. Treatment of uncomplicated acute diverticulitis without antibiotics: a systematic review and meta-analysis. Dis Colon Rectum 2019;62(12):1533-47. DOI: 10.1097/DCR.0000000000001330

17. Desai M, Fathallah J, Nutalapati V, et al. Antibiotics versus no antibiotics for acute uncomplicated diverticulitis: a systematic review and meta-analysis. Dis Colon Rectum 2019;62(8):1005-12. DOI: 10.1097/DCR.0000000000001324

18. Emile SH, Elfeki H, Sakr A, et al. Management of acute uncomplicated diverticulitis without antibiotics: a systematic review, meta-analysis, and meta-regression of predictors of treatment failure. Tech Coloproctol 2018;22(7):499-509. DOI: 10.1007/s10151-018-1817-y

19. Mora-López L, Ruiz-Edo N, Estrada-Ferrer O, et al. Efficacy and safety of nonantibiotic outpatient treatment in mild acute diverticulitis (DINAMO-study). Ann Surg 2021;274(5):e435-42. DOI: 10.1097/SLA.0000000000005031

20. Seta T, Iwagami H, Agatsuma N, et al. Efficacy of antimicrobial therapy in patients with uncomplicated acute colonic diverticulitis: an updated systematic review and meta-analysis. Eur J Gastroenterol Hepatol 2023;35(10):1097-106. DOI: 10.1097/MEG.0000000000002622

21. Dichman ML, Rosenstock SJ, Shabanzadeh DM. Antibiotics for uncomplicated diverticulitis. Cochrane Database Syst Rev 2022;2022(6). DOI: 10.1002/14651858.CD009092.pub3

22. Rezapour M, Ali S, Stollman N. Diverticular disease: an update on pathogenesis and management. Gut Liver 2018;12(2):125-32. DOI: 10.5009/gnl16552

23. Kang G, Son S, Shin YM, et al. Recurrence of uncomplicated diverticulitis: a meta-analysis. Medicina (B Aires) 2022;58(6):758. DOI: 10.3390/medicina58060758

24. Andeweg CS, Mulder IM, Felt-Bersma RJF, et al. Guidelines of diagnostics and treatment of acute left-sided colonic diverticulitis. Dig Surg 2013;30(4-6):278-92. DOI: 10.1159/000354035

25. Binda GA, Cuomo R, Laghi A, et al. Practice parameters for the treatment of colonic diverticular disease: Italian Society of Colon and Rectal Surgery (SICCR) guidelines. Tech Coloproctol 2015;19(10):615-26. DOI: 10.1007/s10151-015-1370-x

26. Andersen JC, Bundgaard L, Elbrønd H, et al. Danish national guidelines for treatment of diverticular disease. Dan Med J 2012;59(5):C4453.

27. Hall J, Hardiman K, Lee S, et al. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Treatment of Left-Sided Colonic Diverticulitis. Dis Colon Rectum 2020;63(6):728-47 DOI: 10.1097/DCR.0000000000001679