ORIGINAL ARTICLE

Intravenous antibiotic therapy after laparoscopic appendectomy in acute complicated appendicitis: the patient clinical response is the key

Terapia antibiótica intravenosa posterior a apendicectomía por laparoscopia en apendicitis aguda complicada: la respuesta clínica del paciente es la clave

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Abstract

Introduction: *The guidelines about acute complicated appendicitis (ACA) recommend 3–5 days of postoperative intravenous antibiotics (IVA). Nevertheless, the time selected by the surgeon can vary according to patient clinical response, ACA type, and professional experience. Once an adequate clinical response is obtained, the change from IVA to oral antibiotic (OA) could be realized without the waiting time established with satisfactory results.* **Objective:** *Determine if a short course of IVA and/or switch to oral route is safe based on the patient clinical response.* **Materials and methods:** *Observational prospective cohort study from a general surgery reference center database since July 2019.* **Results and conclusion:** *48 patients with ACA intraoperative findings were included. Regarding postoperative antibiotic management, only preoperative IVA: 7 (14.58%), IVA 1-3 days: 1 (20.83%), IVA 1-3 days and change to OA: 21 (43.75%), IVA > 3 days: 6 (12.5%), and only OA: 3 (27.08%). The bivariate analysis did not show statistically significant differences in reconsultation (p = 0.81), rehospitalization (p = 0.44), and surgical site infection (p = 0.56) between the antibiotic scheme based on the postoperative clinical response and the traditional one regarding intra-abdominal collection rate, the hospital stays, and hospitalization costs.*

Keywords: *Acute complicated appendicitis. Intravenous antibiotic. Oral antibiotic management. Patient clinical response.*

Resumen

Introduction: *Las guías sobre apendicitis aguda complicada (ACA) recomiendan 3-5 días de antibióticos intravenosos (IVA) postoperatorios. No obstante, el tiempo seleccionado por el cirujano puede variar según la respuesta clínica del paciente, tipo de ACA y experiencia profesional. Una vez obtenida una adecuada respuesta clínica, el cambio de IVA a antibiótico oral (OA) podría realizarse sin esperar el tiempo establecido con resultados satisfactorios.* **Objetivo:** *Determinar si un ciclo corto de IVA y/o el cambio a OA según la respuesta clínica del paciente es seguro.* **Materiales y métodos:** *Estudio observacional de cohorte prospectivo a partir de la base de datos de un centro de referencia en cirugía general desde julio del 2019.* **Resultados y Conclusión:** *Se incluyeron 48 pacientes con hallazgos intraoperatorios de ACA. En cuanto al manejo antibiótico postoperatorio, solo IVA preoperatorio: 7 (14.58%), IVA 1-3 días: 1 (20.83%), IVA 1-3 días y cambio OA: 21 (43.75%), IVA > 3 días: 6 (12.5%) y solo OA: 3 (27.08%). El análisis bivariado no mostró diferencias estadísticamente significativas en la reconsulta (p = 0.81), la rehospitalización (p = 0.44) y la infección del sitio operatorio (p = 0.56) entre el esquema de antibióticos basado en la respuesta clínica postoperatoria y el tradicional con respecto a tasa de colección intrabdominal, estancia hospitalaria y costos de hospitalización.*

Palabras clave: *Apendicitis aguda complicada. Antibiótico intravenoso. Manejo antibiotico oral. Respuesta clínica del paciente.*

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Introduction

Acute appendicitis (AA) is the most common cause of acute abdomen in the world, with an incidence of 5.7-50/100,000 inhabitants per year, with a peak incidence between 10 and 30 years[1,2]. Acute complicated appendicitis (ACA) (perforation, phlegmon, abscess, or peritonitis) and uncomplicated are two entities that require treatments due to the notable difference in complications associated with each other[3,4].

Usually, after surgical management in ACA, additional antibiotic management is provided to prevent or avoid residual infectious complications. In accordance with the guidelines of the Surgical Infection Society and the Infectious Diseases Society of America, an additional 4-7 days of antibiotic are recommended after surgical management in ACA[5]. The latest WSES Jerusalem guidelines for the diagnosis and treatment of AA 2020 update recommend against prolonging antibiotics longer than 3-5 days postoperatively in case of complicated appendicitis with adequate source-control (QoE: High; Strength of recommendation: Strong; 1A) and an early switch (after 48 h) to oral administration of postoperative antibiotics in children with complicated appendicitis, with an overall length of therapy shorter than 7 days (QoE: Moderate; Strength of recommendation: Strong; 1B)[1]. In addition, currently considered the gold standard in the management of AA, laparoscopic appendectomy has already shown to be a protective factor in patients with AA, and it provides clinically beneficial advantages over open method, including shorter hospital stay, decreased need for postoperative analgesia, early food tolerance, earlier return to work, and lower rate of wound infection[5,6]. A recent study questioning whether ambulatory appendectomy should be the standard treatment for AA suggests that this could be considered a standard procedure for both complicated and uncomplicated AA[6].

In most cases of ACA, the treatment length of intravenous antibiotics (IVA) is determined by the surgeon based on the patient's clinical response. Given that not all types of ACA are the same, the study was conducted to identify which patients could be susceptible to switch from IVA to oral antibiotic (OA) after laparoscopic appendectomy in ACA. The hypothesis in mind is considers that once the patient has an adequate clinical response after the procedure, even on an outpatient basis, there is no need to wait 3-5 days of IV antibiotic in safe form while still providing satisfactory outcomes, low complication rates and establish in whom of these are at higher risk of residual infectious complications. This study is carried out to determine if a short course of IVA and/or switch to oral route is feasible and safe based on the patient clinical response and if it increases the risk of intra-abdominal collection and decreases the length of hospital stay or not.

Methods

Study design

A prospective cohort observational study was carried out in a reference center in general surgery since July 2019. A descriptive and bivariate analysis was performed 1 year after the intervention as partial results of a 5-year study. All patients underwent laparoscopic appendectomy with an intraoperative finding of complicated AA. Preoperative antibiotic management was administered in all patients and posteriorly had either a change to OA and outpatient management or continued intravenous scheme based on the intraoperative findings and clinical response of the patient (control of the systemic inflammatory response, oral intake, bowel transit, and pain control).

This project was submitted to the Institutional Review Board, and upon evaluation was granted exemption, as this was a prospective retrospective chart review. The protocol was implemented in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Regarding the inclusion criteria, all patients were older than or equal to 18 years old at the time of the surgery and had undergone laparoscopic appendectomy with intraoperative diagnosis of complicated AA, also, all patients, or their next of kin, provided informed consent before the study inclusion. On the other hand, concerning patients excluded were those who received antibiotic management during the first postoperative month for any other reason than AA or its complications. Other excluded patients included intraoperative suspicion of appendicular neoplasm, chronic or acute malnutrition, and finally, medical failure with antibiotics for AA before surgery.

Intervention

Patients who underwent laparoscopic appendectomy with finding of ACA received preoperative IVA in all cases, a switch to oral OA and outpatient management or prolongation of IVA based on intraoperative findings and clinical response of the patient.

The same antibiotic was used in all patients according to the institutional guidelines for the management of AA, including pregnant patients in whom a safe use of these antibiotics has been proven. The initial antibiotic treatment was 95% of the time a beta-lactam plus a beta-lactamase inhibitor (ampicillin-sulbactam). In the remaining 5% of cases due to penicillin allergy, the antibiotic of choice was clindamycin with aminoglycoside (Amikacin or Gentamicin), and in pregnant patients, this was replaced by metronidazole as the institutional guidelines recommend.

Antibiotics regimens used

1. Only IVA prior to surgery
2. IVA before surgery and switch to oral route
3. Only IVA for 1-3 days
4. IVA for 1-3 days and switch to oral route
5. IVA > 3 days.

Statistical analysis

Clinical findings or characteristics based on the surgical approach were assessed using a Student's t-test and Mann–Whitney U-test or Fisher's test to compare the means between groups for normally distributed and non-normally distributed data, respectively. The χ^2-test was used to compare proportions/frequencies between groups. Primary endpoints were evaluated independently as binary outcomes. Statistical significance was considered $p \leq 0.05$. This study complied with the STROBE guidelines.

Results

A total of 48 patients met the inclusion criteria, 29 patients were women (60%), whereas four of them pregnant, and 19 patients were male (39%). The average age was 34, 4 years old. AA was diagnosed through clinical suspicion (60%), abdominal ultrasound (8%), or computerized tomography scan (27%). The distribution of intraoperative findings is described in Table 1.

Table 1. Description of intraoperative findings

Intraoperative findings	n = 48 (%)
Gangrenous appendix	9 (18.75)
Appendicolith free in abdominal cavity	6 (12.5)
Perforated appendix	21 (43.75)
Localized abscess	12 (25)
Pelvic peritonitis	20 (42.6)
Generalized peritonitis	12 (25)
Phlegmon	23 (47.9)

Table 2. Complications presented with an antibiotic regimen based on the patient's clinical response

Complication	n (%)
SSI grade I	3 (6,25)
SSI grade III	2 (4,16)
Ileus	1 (2)

Peritoneal lavage was not performed in any of the patients, only suction and cleaning. The appendix stump closure technique was polymeric clip 51.4% (or endoloop 37.5%), and also there were used ligasure (56.25%), hook (43.75%), or endobag (39.58%). In the postoperative period, two of the 35 patients presented postoperative ileus and five surgical site infections (SSI), three being superficial and the remaining two organ space (Table 2).

The distribution of antibiotic management and the evaluated postoperative results (complications and length of hospital stay) are described in Tables 3 and 4, respectively.

The descriptive analysis is detailed in Table 5. In the bivariate analysis, no statistically significant difference was found in *reconsultation* (p = 0.81), *rehospitalization* (p = 0.44), and *infection of the surgical site* (p = 0.56) between the traditional scheme or the one based on the clinical response of the patient (Table 6).

Discussion

AA is one of the most common general surgical emergencies worldwide, representing a mortality risk about 8.6% and 6.7%, for men and women, respectively[7,8]. One-third of patients with AA who assist to

Table 3. Distribution of postoperative antibiotic management

Postoperative antibiotic management	n (%)
Only preoperative AB and outpatient management	7 (14.58)
Preoperative IVA and OA	3 (27.08)
IVA 1-3 days only	11 (22.91)
IVA 1-3 days + OA	21 (43.75)
IVA for more than 3 days only	6 (12.5)

Table 4. Length of hospital stay in patients on an antibiotic regimen based on clinical response

Length of hospital stay	n (%)
Ambulatory	11 (22.9)
1 day	12 (25)
2 days	7 (14.5)
3 days	13 (27)
4 days	1 (2)
5 days	2 (4.16)
More than 5 days	2 (4.16)

the emergency service have a complicated appendicitis, which translates into increased risk of postoperative problems, compared to patients with uncomplicated appendicitis[7,8].

Bhangu et al. sustained that the AA may be classified as uncomplicated or complicated. The first one mentioned is about a simple and non-perforated appendicitis, which can be suppurative/phlegmonous, and is less often accompanied by localized or diffuse pus than gangrene; the other one, is a more complex appendicitis, can be gangrenous with friable appendix with purple, green, or black color changes associated with the transmural inflammation and necrosis. This can also perforate, which is not always visible on microscope and finally, abscess may have a pelvic or abdominal location found during examination, in a preoperative imaging or as an operative finding. In the latest WSES Jerusalem guidelines, described that Mällinen et al. argued their hypothesis that the presence of an appendicolith is an independent predictive factor for both perforation and the failure of non-operative management of uncomplicated AA.

The administration of an appropriate antimicrobial therapy, as a precept in gastrointestinal surgery to prevent SSI[8,9]. As is already known, in uncomplicated appendicitis, antimicrobial therapy following surgery is not indicated and can produce adverse events[8,9]. Nevertheless, the time of IVA therapy after laparoscopic appendectomy in complicated appendicitis has not been described. According to the current evidence-based guideline of Jerusalem 2020, the antibiotic regimen is defined by the surgeon and the patient's clinical response, showing that the antibiotic administration, which is about 3-5 days, depends on the source control grade, the appendix aspect, and the degree of peritonitis.

Based on our results, 75% of the patients were managed with an in-hospital stay < 3 days, representing a significant decrease translated to the reduction of hospitalization costs. Compliance rates are similar as expected to the current literature for complicated AA. Saar et al. carried out a controlled trial, with only 24-h antibiotic therapy in a controlled source of a complicated appendicitis, proving safety associated with short length of hospital stay and lower costs[8-11]. de Wijkerslooth et al., carried out a study among 181 patients with gangrenous appendicitis, postoperative antibiotic during less or equal than 24 h in 57 patients (31.5%) and more than 24 h in 124 patients, although there were different factors such as older patients, higher median CRP levels at presentation, and local or diffuse peritonitis during surgery, they showed more infectious complications although not statistically significant, but did correlate with a longer length of stay[12,13].

Additionally, it was observed that of the two patients who developed postoperative abscess, both had in common an appendicolith free in the abdominal cavity as an intraoperative finding. One patient received IVA for 3 days and then OA, whereas the other patient received IVA more than 5 days given a generalized peritonitis, which could explain whether or not this finding constitutes a risk factor for SSI grade III.

Finally, there were no statistically significant differences in *reconsultation* ($p = 0.81$), *rehospitalization* ($p = 0.44$), and SSI ($p = 0.56$) between the traditional scheme or the one based on the patient clinical response. The main limitation in the study design is data without a larger sample needed to confirm the hypothesis; however, it has shown promising results. The previous limitation could be minimized by performing a randomized clinical trial to evaluate safety

Table 5. Descriptive analysis

Variable name	n (%)	Median	Interquartile range
Gender	Woman 29 (60) Man 19 (39)	-	-
Age	-	31	16.5
Body mass index	-	27.2	5.05
Clinical diagnosis	No 19 (39) Yes 20 (60)	-	-
Ultrasound diagnosis	No 44 (91) Yes 4 (8)	-	-
Tomography computerized diagnosis	No 35 (72) Yes 13 (27)	-	-
Pregnant	No 44 (91) Yes 4 (8)	-	-
Evolution timeline (hours)	-	3.0	2.0
Leukocytes	-	1548	5854
Gangrenous appendix	No 39 (81.25) Yes 9 (18.75)	-	-
Appendicolith into the abdominal cavity	No 42 (87.5) Si 6 (12.5)	-	-
Perforated appendix	No 27 (56.25) Si 21 (43.75)	-	-
Perforation	No 46 (95.83) Yes 2 (4.16)	-	-
Localiced abscess	No 36 (75) Yes 12 (25)	-	-
Pelvic peritonitis	No 28 (58.33) Yes 20 (41.66)	-	-
Generalized peritonitis	No 36 (75) Yes 12 (25)	-	-
Appendiceal phlegmon	No 25 (52.08) Yes 23 (47.91)	-	-
Ligasure	No 21 (43.75) Yes 27 (56.25)	-	-
Hook	No 27 (56.25) Yes 21 (43.75)	-	-
Endobag	No 29 (60.41) Yes 19 (39.58)	-	-
Drain	No 40 (83.33) Yes 8 (16.66)	-	-
Hemolock	No 22 (45.83) Si 26 (54.16)	-	-
Endoloop	No 30 (62.5) Yes 18 (37.5)	-	-
Peritoneal lavage	No 48 (100) Yes 0	-	-

(Continues)

Table 5. Descriptive analysis *(continued)*

Variable name	n = (%)	Median	Interquartile range
Postoperative ileus	No 46 (95.83) Yes 2 (4.16)	-	-
SSI	No 43 (89.58) Superficial 3 (6.25) Organ-espace 2 (4.16)	-	-
Length of hospital stay	-	1.0	3.0
Duration of postoperative hospital stay (days)	0: only preoperative antibiotic 7 (14.58) 1: intravenous antibiotic 1-3 days 1 (20.83) 2: intravenous antibiotic 1-3 days and switch to oral antibiotic administration 21 (43.75) 3: intravenous antibiotic more than 3 days 6 (12.5) 4: only oral antibiotic 3 (27.08)	-	-
Outpatient antibiotic treatment	No 8 (16.66) Yes 40 (83.33)	-	-
Reintervention	No 48 (100) Yes 0	-	-
Reconsultation	No 44 (91.66) Yes 4 (8.33)	-	-
Rehospitalization	No 46 (95.83) Yes 2 (4.16)	-	-

SSI: surgical site infection.

Table 6. Bivariate analysis

Outcomes	0	1	2	3	4	p-value
Reintervention	0	0	0	0	0	0
Reconsultation	0	0	2	1	1	0.81
Rehospitalization	0	0	1	1	0	0.44
Infection of the surgical site	0	0	2	3	0	0.05

0: only preoperative antibiotic; 1: intravenous antibiotic 1-3 days; 2: intravenous antibiotic 1-3 days and switch to oral antibiotic administration; 3: intravenous antibiotic more than 3 days; 4: only oral antibiotic.

and effectiveness of the different treatment regimens.

Conclusion

The use of an antibiotic regimen based on the postoperative clinical response of the patient turned out to be effective and safe after laparoscopic appendectomy for complicated AA. There were no statistically significant differences between the traditional scheme and the scheme based on the postoperative clinical response of the patient in the intra-abdominal collection rate. The antibiotic scheme based on the postoperative clinical response of the patient could decrease the time of hospital stay and consequently the reduction of hospitalization costs based on the above.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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