

COMPARISON BETWEEN SURGICAL AND CONSERVATIVE TREATMENT FOR ACUTE APPENDICITIS: A SYSTEMATIC REVIEW

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Abstract: Acute appendicitis is one of the main reasons for emergency abdominal surgery, culminating in appendectomy. However, articles on clinical trials and systematic reviews analyzing the non-surgical treatment of appendicitis have been published, indicating that it may be a viable option in uncomplicated cases. However, in practice, in Brazil, these cases are almost always treated surgically, which is one of the most frequently performed interventions in the emergency room. Thus, the objective was to verify whether conservative treatment for acute appendicitis can already be considered as a substitute for surgery in cases of uncomplicated acute appendicitis. A systematic review of the literature was carried out, whose research was carried out in clinical trials, published between 2017-2022, that compared results of surgical and conservative treatments for acute appendicitis. The databases were PubMed, SciELO and Virtual Health Library. Fifteen articles were selected, which revealed that there are still controversial results regarding conservative treatment, but that even so it is quite effective in certain cases. Even though some studies have shown high rates of recurrence, these did not exceed 50%. Therefore, more than 50% of surgeries that would have been unnecessary, whose treatment with antibiotics alone offered remission of the disease, were avoided. What can be observed is that in order to have better success rates with conservative management, it is necessary to establish more robust characterization parameters on the target population for this treatment. In that regard, it was observed that higher rates of recurrence are associated with the presence of appendicitis and severe pain reported by the patient at presentation. It is suggested that these characteristics be considered as exclusion factors for the option for conservative treatment. Because there are significant rates of recurrence, it cannot be said

that the therapeutic approach is equivalent to appendectomy in treatment success, but rather that it is a viable option and that it must be considered.

Keywords: Appendicitis; treatment; quality of life.

INTRODUCTION

Appendicitis is inflammation of the appendix, a small organ located in the first portion of the large intestine. It is a common gastrointestinal disease that affects approximately 1 in 1,000 people per year in the Western world, with the highest incidence between the ages of 10 and 19 years. Historically, it was based on the assumption that appendicitis is an irreversible progressive disease, which culminates in perforation of the appendix, causing subsequent peritonitis. Because of this, its standard treatment is appendectomy, as it has always been considered necessary to remove the inflamed appendix as soon as possible when there is suspicion of appendicitis. [1]

Acute appendicitis is one of the most common reasons for emergency abdominal surgery. Although appendectomies (whether open or laparoscopic) are considered safe and simple procedures, it is a fact that surgical management is associated with several problems. Complications related to surgery or anesthesia occur in up to 10% of children and adolescents who undergo appendectomy. [two]

For many years, laparotomy remained the “gold standard”. With the introduction of laparoscopic access in 1982, its use became widespread and proved to be as safe and efficient as conventional access. In 2004, endoscopic surgery through natural orifices emerged, evolving in 2007 to the single-track modality and, in 2015, to retrograde endoscopy. For each of these methods, the evolution of the clinical condition is variable,

and may or may not develop favorably, leading to the development of new treatment options. In this scenario, conservative treatment, followed or not by interval surgery, is an option that has been proposed in order to avoid unnecessary surgical interventions, which have similar morbidity and mortality to those performed in emergencies. [3]

At the same time, the progressive nature of appendicitis began to be questioned, leading to the classification of two types of appendicitis: uncomplicated, which does not tend to perforate; and the complicated one, whose exams show a tendency to perforation. As a result, the need for an appendectomy became increasingly questioned. [1] Even because, uncomplicated appendicitis, besides being able to be cured only in treatment with antibiotics, can also resolve spontaneously, without treatment. [4]

Articles of clinical trials analyzing the non-surgical treatment of appendicitis were published and then systematic reviews were carried out evaluating these results, as is the case of the study by Mosuka et al. [2], who included 12 studies in their research, concluding that antibiotic therapy, in addition to being more economical, can be administered safely in a small subset of individuals with uncomplicated appendicitis. Besides, Sippola et al. [5] stress the issue that antibiotic therapy for uncomplicated acute appendicitis is associated with substantial savings.

Currently, it is already considered that the treatment of acute appendicitis must not be surgical in all cases, and that a conservative treatment can be chosen. [3] Due to this, the non-surgical treatment of uncomplicated appendicitis is gaining more and more space in developed countries, being performed with intravenous (IV) administration of antibiotics and clinical monitoring. [1]

JUSTIFICATION

There are already several studies that bring results on the effectiveness of therapy with antibiotics alone for acute appendicitis. However, in practice, in Brazil, these cases are almost always treated surgically, which is one of the most frequently performed interventions in the emergency room. This fact, together with the large number of cases of the disease and the high number of surgeries performed, justify the importance of this study, because by gathering results from clinical studies that allow comparing the effectiveness of both treatments, it is intended to provide more solid evidence. for the medical community, on which professionals can base themselves when making a decision about which treatment to choose.

In addition, even though the option for non-surgical treatment has already been occurring in many countries, there is questioning by the scientific community, due to the lack of controlled and randomized clinical trials, comparing treatment based only on antibiotics with appendectomy. However, in recent years these studies have been carried out, which reinforces the importance of analyzing their results in a new systematic review.

OBJECTIVES

GENERAL OBJECTIVE

To verify whether conservative treatment for acute appendicitis can already be considered as a substitute for surgery in cases of uncomplicated acute appendicitis.

SPECIFIC OBJECTIVES

- Select articles from clinical trials comparing results on surgical and conservative treatment of acute appendicitis;
- Gather and analyze the results of these studies;

- To compare the results of conservative and surgical treatments, to see whether antibiotic treatments have shown efficacy and safety comparable to surgical ones.

LITERATURE REVIEW

The first description of acute appendicitis was made in 1886 by Reginald Fitz and, since then, it has continued to be the most frequently attended intra-abdominal surgical emergency in hospitals, with an incidence ranging from 13 to 40% between studies. It is estimated that between 7 and 12% of the world's population will develop it at some point in their lives, and it can occur at any age, but it is predominant between the second and third decades, and is more common in males. [3]

Its diagnosis involves medical history, physical and laboratory examinations, and abdominal ultrasound. If the latter is insufficient, computed tomography or magnetic resonance imaging can be performed. These tests are important not only to define the diagnosis, but also to classify appendicitis as uncomplicated or complicated. Anyway, in both types of appendicitis, the decision for surgical or conservative treatment must be based on the general clinical picture and the patient's risk factors. [6]

Appendectomy is the treatment of choice in the vast majority of cases, but it causes major complications, being associated with intra and postoperative morbidities, including vascular lesions, urinary tract complications, hematomas, colonic fistulas, surgical site infections, adhesions, obstructions bowel movements and significant length of hospital stay. Postoperative complication rates range from 2% to 23%, and more than 3% of patients are readmitted with bowel obstruction and postoperative compliance. [7]

To alleviate these complications, endoscopic retrograde appendicitis therapy (ERAT) was developed, which is an emerging

modality of endoscopic treatment for uncomplicated acute appendicitis. In this modality, due to a concern about the future risk of malignancy in children from ionizing radiation, contrast-enhanced ultrasound may be used instead of endoscopic retrograde appendicular radiography. [8]

However, whatever the method, surgery can bring about greater complications, making antibiotic therapy an alternative treatment, especially in uncomplicated cases or in cases where surgery is contraindicated. [7]

Antibiotic regimens for the treatment of appendicitis can be classified into three categories: those that include a carbapenem; those that include a cephalosporin; and those that include a β -lactam/ β -lactamase inhibitor combination. [9]

Studies have been published showing positive results with the conservative treatment of appendicitis. For example, in a prospective multicenter cohort in the Netherlands, data from 45 children aged 7 to 17 years who were treated without surgery for uncomplicated appendicitis were analyzed. Of these, 42 (93%) were discharged after one day of treatment, with resolution of clinical symptoms, without the need for an appendectomy. [1]

Therefore, the result of this study suggests that non-operative treatment is a viable alternative to appendectomy, promoting clinical recovery with antibiotic therapy alone. However, this cited study did not use a control group or compare results with an appendectomy group. The one performed by Park et al. [4] was a randomized study that compared the outcome of a non-antibiotic management strategy (control group) with that of antibiotic therapy in uncomplicated appendicitis. Their results indicated that treatment failure rates were similar between groups, so there was no superiority of antibiotic treatment over spontaneous recovery from the disease.

Besides, in the study by Poprom et al. [7], who analyzed nine randomized controlled trials (RCTs), the authors claim that, even though positive results have been found with β -lactamase, appendectomy is still the most effective treatment for uncomplicated appendicitis.

It is because of results like these that the effectiveness of antibiotics in appendicitis remains controversial, making many physicians not confident in prescribing antibiotics as a first-line treatment. [7] Therefore, it is important to investigate the effectiveness of the non-surgical management of appendicitis in studies that compare the results of the two treatment approaches (non-surgical and surgical), which is what this research proposes.

METHODOLOGY

A systematic review of the literature was carried out, whose research was carried out exclusively in clinical trials, randomized or not, that compared results of surgical and conservative treatments for acute appendicitis. The aim was to gather these results in a single study, comparing the effectiveness of both, to verify whether it is already possible to point to conservative treatment with antibiotics as a substitute for surgery in cases of uncomplicated acute appendicitis.

Articles were searched in the following online databases: Medline/PubMed; SciELO; Virtual Health Library (VHL). The search for articles was performed using the following combination of descriptors, with the Boolean AND operator: (acute appendicitis) AND (surgical treatment) AND (antibiotic). Some selection filters were established as inclusion criteria: Full availability of the text; clinical trials or randomized controlled trials only; published in the last five years (2017-2022); in English, Spanish and Portuguese. Exclusion criteria will be review articles, case reports

or with methodologies other than clinical studies; and studies that do not bring results comparing treatments for acute appendicitis.

After the presentation of the articles by the databases, already pre-selected through the filters applied as inclusion criteria, a new pre-assessment was made through the titles and abstracts of the publications. The articles that went through this stage were read in full, resulting in the choice of those that effectively brought data of interest to this work. The result of this selection of articles and the data of each one of them in tabular form are presented in the next section of this study.

RESULTS AND DISCUSSION

The search resulted in 39 clinical/randomized articles in PubMed, of which 12 were chosen; in 4 articles in Scielo, but none were selected; and 37 articles in the VHL, however many in duplicate with the previous ones, being selected more 3 articles, totaling the choice of 15 clinical articles to compose this study.

To analyze the results of these 15 clinical trials, a comparative table was developed (Table 1), where the following information is broken down: identification of the study by the name of the authors and year of publication; age range of patients; how many underwent appendectomy; how many underwent antibiotic therapy; and the results found.

| Study | Age range | Appendectomy | Antibiotic therapy | Results |
|--------------------------------------|-----------------|--------------|--------------------|--|
| Ali et al., 2021 [10] | 18-65 years old | 159 | 159 | Antibiotics were vastly more cost-effective than appendectomy and promoted better quality of life outcomes for patients. |
| Allievi et al., 2017 [11] | ≥18 years | 109 | 284 | Conservative management proved to be as safe and effective as surgery, and patients treated conservatively had shorter hospital stays. |
| CODA Collaborative et al., 2020 [12] | ≥18 years | 776 | 776 | Antibiotics were not inferior to appendectomy, as both groups had similar results in the first 30 days. However, about 30% of those who received antibiotics required a posterior appendectomy within 90 days. |
| CODA Collaborative et al., 2021 [13] | ≥18 years | 776 | 776 | Long-term results of the previous study. The percentage of patients undergoing subsequent appendectomy was 40% at 1 year, 46% at 2 years, and 49% at 3 and 4 years. Still, a substantial number of patients report a preference for antibiotics, even if appendectomy is required later. |
| Haijanen et al., 2019 [14] | 18-60 years | 273 | 257 | At a 5-year follow-up, antibiotic treatment resulted in significantly lower overall costs compared with appendectomy. And the majority (61%) of patients in the antibiotic group did not undergo appendectomy in this follow-up. |
| Minneci et al., 2020 [15] | 7-17 years | 698 | 370 | Preliminary results show that conservative treatment with antibiotics had a success rate of 67.1% and, compared with urgent surgery, was significantly associated with fewer days of disability. |
| Minneci et al., 2021 [16] | 7-17 years | 698 | 370 | Long-term results of the previous study. At 1-year follow-up, conservative treatment was successful for 63.8% of patients aged 10 years and younger versus 68.1% of patients older than 10 years, and led to fewer days of disability compared with appendectomy laparoscopic. |
| Minneci et al., 2022 [17] | 7-17 years | 698 | 370 | In a subsequent analysis of the study above, it was identified, in relation to patients who failed conservative treatment, that this risk was related to greater pain reported by the patient at presentation. But there was no increased risk of failure associated with age, white blood cell count, sex, race or ethnicity. |
| Monsell et al., 2022 [18] | ≥18 years | 776 | 776 | In analysis of data from the CODA study, the presence of an appendicitis was found to be associated with an almost 2-fold increased risk of undergoing appendectomy within 30 days of starting antibiotics. |

| | | | | |
|-----------------------------|-----------------|-----|-----|--|
| O'Leary et al., 2021 [19] | ≥16 years | 93 | 93 | Patients with uncomplicated acute appendicitis treated with antibiotics alone have high recurrence rates and poorer quality of life. |
| Patkova et al., 2020 [20] | 5-15 years | 26 | 24 | At 5 years of follow-up, 46% of children treated with antibiotics for acute non-perforated appendicitis underwent appendectomy. There were no failures in the appendectomy group. |
| Poillucci et al., 2017 [21] | 18-65 years old | 184 | 162 | Conservative treatment was less successful than surgical treatment, but was able to prevent appendectomies in about 80% of patients who left the hospital with clinical recovery with antibiotics alone. |
| Prechal et al., 2019 [22] | ≥18 years | 70 | 34 | Treatment success at a 1-year follow-up was 77.1% for the antibiotic group and 100% for the surgical treatment group. |
| Salminen et al., 2018 [23] | 18-60 years | 273 | 257 | Among patients who were initially treated with antibiotics, the probability of late recurrence at 5 years was 39.1%, which supports the feasibility of antibiotic treatment as an alternative to surgery for uncomplicated acute appendicitis. |
| Sippola et al., 2017 [24] | 18-60 years | 273 | 257 | Analyzing the same sample from the study above, it was identified that patients who received antibiotic therapy for uncomplicated appendicitis had lower costs than those who underwent surgery. |

Table 1 - Clinical trials comparing appendectomy x antibiotic therapy

Most clinical articles brought important information about the efficacy and advantages presented by conservative treatment with antibiotics. Even though some of them have pointed out some rate of recurrence in some patients [12] [13] [19] [20] [21] [22] [23], they also observed advantages in other variables, such as cost, recovery time and quality of life.

Another observation made is that even with reasonable recurrence rates, but varying between studies, there is no denying that conservative treatment with antibiotics is associated with shorter hospital stay and faster return to normal activities, in addition to preventing appendectomies in a number of cases. considerable number of patients, who leave the hospital with clinical recovery and do not present recurrences. [21]

For some studies [11] [14] [15] [16] [17]

[21] [22] [23], it was proven that conservative treatment can be considered effective and safe for selected cases of uncomplicated acute appendicitis, whose clinical presentation is often well controlled by antibiotic therapy.

But, there was also a study that did not find favorable results [19], stating that patients with uncomplicated appendicitis treated with antibiotics not only have high rates of recurrence but also follow with a lower quality of life, indicating that the appendectomy must be maintained. as the mainstay of treatment for the disease.

Among the selected studies there was one that evaluated a larger amount of patients, all over the age of 18. This is a multicenter randomized study, initiated in 2016, called Comparison of Outcomes of Antibiotic Drugs and Appendectomy (CODA) [12] [13]

[18], in which the researchers compared the short- and long-term outcomes of surgical versus conservative treatment. In total, data from 1,552 adults were analyzed, 414 of these with appendicolith (calcified deposit within the appendix). There was no significant difference in outcomes, but in the antibiotic group, nearly 3 out of 10 participants required subsequent appendectomy within 90 days. Among them, the patients with appendicolith were the ones who had a higher risk of appendectomy and complications than the others. [12] This fact is important, because it is a complication that offers a higher risk of recurrence of appendicitis, and may have negatively influenced the results of the study.

Besides, in the same study, but in a later publication [13], long-term data showed that there were high rates of recurrence (49% of patients, in a 4-year follow-up) that led to the option for appendectomy, which was more common among patients who had appendicitis, even though this increased risk has been attenuated over time. In addition, in a new analysis of the data from the same study [18], it was found that the presence of an appendicitis exacerbates twice as much the risk of failure to manage with antibiotics, leading the patient to appendectomy within 30 days after the start of treatment.

However, it is important to emphasize that even with the subsequent need for surgery, many patients reported their preference for starting with conservative treatment with antibiotics. [13] This is an interesting issue to emphasize that decision-making about treatment must be shared between physicians and their patients, as the latter have the right to participate in this choice.

In another large multicenter randomized study [15] [16] [17], with 1,068 patients aged between 7 and 17 years, therefore, children and adolescents, the results were more positive, with a success rate of 67.1% for the treatment of

uncomplicated appendicitis which, compared with surgical treatment, was statistically and significantly associated with fewer days of disability over the one-year follow-up period. In a subgroup analysis [16], it was found that the success rate of antibiotic therapy and its association with fewer days of disability than surgery in children did not differ by age or family income. Still in relation to the same study sample, but in a later analysis [17], it was also identified that there was no increase in the risk of treatment failure associated with age, white blood cell count, sex, race and ethnicity, but rather with increased patient-reported pain at presentation, which was associated with increased risk of conservative treatment failure and need for appendectomy.

Regarding costs, three studies [10] [14] [25] compared treatment with antibiotics alone versus appendectomy in the treatment of uncomplicated acute appendicitis, proving that those who received antibiotic therapy had lower costs than those who underwent surgery, being widely more cost-effective, in addition to leading to better quality of life outcomes for patients. These are two points that are very favorable to the choice of conservative treatment with antibiotics, which justify the inclusion of this treatment as a first-line choice.

Therefore, although there are controversial results brought by some studies, antibiotic treatment of appendicitis is now described as an “accepted first-line treatment” by the American College of Surgeons, for uncomplicated acute appendicitis. [13]

FINAL CONSIDERATIONS

Appendectomy is still the option of choice and the gold standard for the treatment of complicated appendicitis, but in uncomplicated cases, the option for treatment with antibiotics is already a reality that must be better explored for certain groups of patients.

This treatment offers a shorter hospital stay, faster recovery and better quality of life, in addition to a lower financial burden. It also shows higher rates of choice preference by patients and greater satisfaction.

Even though some studies have shown high rates of recurrence and the need to perform a posterior appendectomy, these rates did not exceed 50%. Therefore, more than 50% of surgeries that would have been unnecessary, whose treatment with antibiotics alone offered remission of the disease, were avoided. On the other hand, because of these significant rates of recurrence, it cannot be said that the therapeutic approach is equivalent to appendectomy in treatment success, but rather that it is a viable option and that it must be considered.

What can be observed in the evaluated clinical trials is that in order to have better

success rates with conservative management, it is necessary to establish more robust characterization parameters on the target population for this treatment.

It is suggested, therefore, that further research be carried out, seeking to establish which patient characteristics indicate those who must be candidates for non-surgical treatment. As in one of the studies analyzed, it was observed that the rates of appendicitis recurrence and need for appendectomy were higher among those with appendicitis, while another study indicated that the presence of severe pain reported by the patient at presentation is associated with an increased risk of failure in the procedure. treatment with antibiotics, these characteristics could be considered as exclusion factors for the option for conservative treatment.

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