Non-operative Management of Acute Appendicitis in Pediatric Population: A Narrative Review

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Abstract:

Background and Objective: Acute appendicitis is traditionally treated with operative approaches. The latest progress in diagnostic techniques has coincided with the introduction of novel non-invasive treatment options. Original studies on this subject indicate that non-operative management of acute appendicitis in the children population is feasible. This review explores current literature on the efficacy, safety, and long-term outcomes of non-operative treatments and gives an overview of this management method.

Materials & Methods: In the pursuit of conducting this narrative review, a systematic search was performed utilizing the Scopus, Embase, ISI, and Google Scholar databases. The inclusion criteria comprised original articles, review papers, and meta-analyses that focus on the non-surgical treatment of acute appendicitis in the pediatric population. This investigation adopted a descriptive-analytical approach. All pertinent literature was meticulously evaluated, and data were carefully extracted; the findings and insights obtained from these sources were subsequently incorporated into various sections of this review.

Results: Non-operative management has been reported to have a lesser length of hospital stay and a better patient satisfaction rate in comparison to operative management. Key factors in selecting the appropriate patients for non-operative management include younger age, lesser symptoms and fever durations, mild clinical presentations, lower white blood cell and CRP levels on laboratory studies, and lower appendix diameter on imaging. Further Randomized Controlled Trials with longer follow-up durations and similar antibiotic administration are required to address the heterogeneity of previous research.

Conclusion: Existing evidence from previous studies advocates for the non-surgical management of uncomplicated acute appendicitis in children. However, it is imperative to establish comprehensive guidelines for patient selection. Such guidelines are essential to mitigate the risk of misdiagnosis and to prevent the occurrence of serious complications stemming from inadequate management.

Keywords: *Pediatrics, Acute Appendicitis, Antibiotics, non-operative management, appendectomy*

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Background and Objective

Acute appendicitis represents the most prevalent condition among children that necessitates urgent assessment.[1] Despite recent studies indicating a decline in the overall incidence of this condition, it remains most frequently observed in children aged 10 to 19 years.[2,3] The diagnostic process for appendicitis in this age group is particularly complex, as factors such as ineffective communication, symptoms overlapping with other medical issues, and the limitations of physical examinations can contribute to both misdiagnosis and delays in appropriate treatment.[4]

The standard treatment option for acute appendicitis is appendectomy.[5] However, surgical intervention can be discouraging for pediatric patients and their families, particularly considering the associated costs and complications.[6,7] However, recent advancements in diagnostic techniques and an enhanced understanding of the disease's natural progression have increased the interest in Non-Operative Management (NOM) strategies. Consequently, the management of acute appendicitis has undergone significant evolution, reflecting a shift towards exploring alternative therapeutic options.[8]

This narrative review aims to synthesize the current literature on the NOM of acute appendicitis in children, examining its efficacy, safety, and long-term outcomes. The article aims to provide a comprehensive overview of the non-operative approach in the management of acute appendicitis.

1. Pathophysiology

Acute appendicitis, the most common surgical emergency among children, is marked by the inflammation of the vermiform appendix.[3] The onset of appendicitis is frequently attributed to the obstruction of the appendiceal lumen, which may arise from various factors such as fecaliths, lymphoid hyperplasia, foreign bodies, or neoplasms.[9,10] This obstruction triggers an increase in intraluminal pressure, thereby impairing blood flow and causing ischemic changes in the appendiceal wall.[11,12] Historical research has consistently indicated a significant correlation between the presence of fecaliths and the occurrence of appendicitis, reinforcing the obstruction theory.[13] In addition, findings from the study by Rogers et alsuggest that the appendiceal environment contains unique microbial communities that may play a significant role in the development of appendicitis, such as the species of Fusobacterium.[14]

The inflammatory process can progress through several stages: Initially, patients often report pain localized around the peri-umbilical region, which arises from the stimulation of visceral nerves.[12] This initial discomfort is an early indicator of the underlying pathological changes within the abdominal cavity. As the condition progresses, the inflammatory response can escalate, potentially involving structures beyond the appendix. This extension of inflammation may impact the parietal peritoneum, resulting in a more pronounced clinical presentation characterized by symptoms such as fever, nausea, and vomiting.[10,11] If the inflammatory process remains unaddressed, it can lead to perforation of the appendix, a complication that significantly increases the risk of morbidity and mortality.[12]

2. Evolution of treatment options

The approach to managing acute appendicitis has undergone considerable transformation throughout history, shifting from conventional surgical practices to more sophisticated methodologies. The surgical intervention for appendicitis can be traced back to the 18th century, marked by the resection of the cecal appendix trapped in an inguinal hernia conducted by Claudius Amyand in 1735.[15]

The late 19th century marked a pivotal moment in standardizing surgical procedures. In 1894, Charles McBurney introduced the open appendectomy (OA) technique, characterized by a substantial incision in the right lower quadrant of the abdomen.[16] This method established itself as the gold standard for an extended period,

facilitating direct access to the inflamed appendix. The development of laparoscopic surgery in the 1980s contributed to the widespread adoption of laparoscopic appendectomy (LA) as the favored surgical method, primarily because of its minimally invasive characteristics. This approach is associated with reduced postoperative discomfort, decreased duration of hospital admission, and expedited recovery periods. Laparoscopic appendectomy is characterized by the use of smaller incisions and the incorporation of a camera, which enhances visualization during the procedure.[17] In recent years, the technique of single-incision laparoscopic appendectomy (SILA) has gained prominence. This method employs a solitary incision, usually located at the umbilicus, to achieve superior cosmetic results and minimize complications. While SILA is still undergoing refinement, it signifies a notable progression in surgical methodologies.[18]

Alongside surgical interventions, there is an increasing focus on NOM for uncomplicated appendicitis, predominantly utilizing antibiotics. Research indicates that this method can be successful, decreasing the necessity for surgical procedures in numerous instances.[19] Current management strategies for acute appendicitis are now more personalized, taking into account variables such as the patient's overall health status, the severity of the appendicitis, and any existing complications.[20]

3. Non-Operative Management approaches

Non-surgical management of acute appendicitis predominantly focuses on the administration of antibiotics alongside supportive care measures. Numerous studies have highlighted several essential strategies that contribute to the effectiveness of this treatment modality.

Individuals need to be hospitalized for observation and be provided with supportive treatment such as intravenous fluids, pain relief medications, and antibiotics. This method may result in the natural resolution of less severe instances of appendicitis.[21]

Research findings demonstrate that antibiotics as an initial and standalone approach, can successfully address acute uncomplicated appendicitis.[22] Commonly recommended treatment protocols typically involve the use of broad-spectrum antibiotics, including amoxicillin-clavulanic acid, piperacillin-tazobactam, or ceftriaxone in conjunction with metronidazole.[23] For example, Perveen et al prescribed Cefotaxim 100 mg/kg/24h along with Metronidazole 30 mg/kg in 3 doses per day in their study while Abbo et al treated the patients with intravenous Amoxicillin and Clavulanic acid (100 mg/kg/day) for 2 days (six doses).[24,25]

NOM may also include oral antibiotics after initial improvement. A regimen might involve administering intravenous antibiotics for 48-72 hours, followed by a course of oral antibiotics for a total of 7 days.[23]

Patients undergoing non-operative treatment are closely monitored for any signs of deterioration.[22,24] If symptoms worsen or do not improve, an appendectomy may be performed.[26]

4. Efficacy and safety of non-operative Treatments

The administration of NOM through antibiotic therapy has been accompanied by a success rate ranging from 63% to 80% over one year, depending on the particular study and the demographic characteristics of the patient population involved.[27,28] For example, findings from the NOTA study revealed a recurrence rate of less than 14% after a two-year follow-up period.[28] Tan et al study revealed a recurrence rate of about 24% in 16 months.[29] A comprehensive meta-analysis has shown that the initial administration of antibiotics effectively treats 97% of pediatric cases with uncomplicated appendicitis, while the recurrence rate is approximately 14%.[30]

Short-term outcomes: The majority of clinical symptoms tend to improve rapidly, often within a single day following the initiation of non-operative treatment. Research indicates that pain levels show a marked reduction after just one day of therapy, with most pediatric patients

experiencing relief from nausea and vomiting.[31] The Appendicitis Acuta (APPAC) trial further supports the efficacy of NOM by revealing that it is linked to a reduced number of days lost to disability when compared to surgical options.[32,33]

Long-term outcomes: Long-term observational studies have demonstrated that a considerable number of children who initially receive non-operative treatment for appendicitis may later experience a recurrence of the condition. However, it should be emphasized that a considerable proportion of these cases can be managed successfully with conservative treatment options. Thereby avoiding the necessity for surgical intervention. For example, research has shown that approximately 14% of pediatric patients who underwent NOM ultimately required an appendectomy due to recurrent appendicitis.[30] However, a systematic review conducted by Decker et al. identified a failure rate of 32% after one year or more, suggesting that a considerable number of children might ultimately necessitate surgical intervention.[32]

Complications and safety: Evidence indicates that NOM is a safe approach, as the studies report no fatalities associated with this treatment method.[27] The incidence of complications linked to NOM tends to be low; however, the potential for severe complications arising from appendicitis itself continues to be a significant concern.[26,32] The presence of an appendicolith has been identified as a risk factor for treatment failure, suggesting that careful patient selection is crucial for the success of NOM.[21,34,35]

5. Comparison of non-operative and operative treatments

ü Efficacy:

Appendectomy remains the gold standard for treating appendicitis, with a success rate of nearly 100%. In the APPAC trial, 99.6% of patients who underwent appendectomy had successful outcomes.[33] NOM with antibiotics has shown varying success rates. For instance, in the APPAC trial, 72.7% of patients treated with antibiotics did not require surgery within one year.[33] However, other studies report success rates ranging from 67% to 88% for NOM.[36,37] According to a meta-analysis of 16 studies, non-operative treatments achieved an efficacy rate of 92%.[38]

ü Complication Rates:

The complication rate for appendectomy can be significant, with studies reporting rates of 20.5% for minor complications, 2.8% for major complications, and 24.4% for the overall complication rate at five years.[39] NOM does not have surgically related complications.[34] The APPAC trial reported a complication rate of only 2.8% in the antibiotic group.[33] In a study focusing on NOM, complications were noted in 20.8% of patients, but most were not severe.[26] However, findings from a meta-analysis demonstrated that antibiotics resulted in a considerably reduced rate of uncomplicated recovery compared to surgical procedures.[40] Another meta-analysis by Maita et al. demonstrated no significant difference in the rates of complications when comparing nonoperative treatment to surgical intervention. However, they suggested NOM as a safe and effective approach for nonperforated acute appendicitis in selective pediatric patients.[38]

ü Length of Hospital Stay:

Patients undergoing appendectomy typically have a longer hospital stay. In Svensson's study the median length of stay for surgical patients was reported as 34.5 hours and in Wolferstetter's study, this length was 4.5 days.[21,41] Patients treated non-operatively often have shorter hospital stays. In the APPAC trial, the median length of stay for the antibiotic group was longer due to monitoring protocols, but it is generally shorter in practice.[33] However, a meta-analysis demonstrated no significant difference in the length of hospital stays for patients treated with non-operative methods compared to those who underwent surgical procedures.[38]

ü Recovery Time and Disability Days:

Patients who undergo surgery may experience longer recovery times, with an average of 10.9 disability days reported. NOM is associated with fewer disability days, averaging around 6.6 days. Patients often return to normal activities more quickly.[36]

ü Patient Satisfaction and Quality of Life:

While surgery is effective, some patients may experience dissatisfaction due to complications or longer recovery times. Many patients and families express a preference for NOM due to the avoidance of surgery and its associated risks. Studies indicate that patient satisfaction is generally high with NOM, especially when it is successful.[37,42]

ü Recurrence Rates:

Recurrence is not a concern post-appendectomy, as the appendix is removed. Recurrence rates for NOM can be significant, with studies reporting rates of 27% to 39% within one year.[21,39] In situations where recurrence occurs, the preferred initial intervention would be an appendectomy.[27]

6. Patient Selection Criteria

To ascertain the most appropriate candidates who benefit from non-operative intervention in cases of uncomplicated appendicitis among children, it is essential to analyze a range of clinical, demographic, and laboratory considerations. Evaluating the following factors can help in selecting appropriate candidates:

1. Age: Candidates should typically be older than 7 years. Younger children may present with more severe symptoms and complications, making them less suitable for NOM.[43]

2. Duration of Symptoms: A shorter duration of symptoms (ideally less than 48 hours) is favorable. Studies indicate that children with symptoms lasting less than 24 hours have better outcomes with NOM.[43-45]

3. Fever Duration: Candidates should ideally have a shorter duration of fever prior to admission. A fever lasting less than 1 day is associated with a higher likelihood of successful NOM.[43,45]

4. Clinical Presentation: Patients should present with mild symptoms, such as localized abdominal pain without significant rebound tenderness or signs of systemic infection. The absence of severe abdominal pain or peritonitis is crucial.[46]

5. Laboratory Findings:

- White Blood Cell Count (WBC): A lower WBC count (ideally less than 10,000/μL) is preferable, as higher counts may indicate a more severe inflammatory process.[36,44-46]
- C-Reactive Protein (CRP): Lower CRP levels are also associated with better outcomes in NOM.A C-reactive protein (CRP) level of approximately 15 or less has been linked to successful NOM.[45,46]

6. Imaging Findings: The absence of an appendicolith and a smaller appendiceal diameter are important factors. Larger diameters (generally more than 10.5) and the presence of an appendicolith are associated with higher failure rates of NOM.[35,45,46]

7. Parental Consent and Preference: Involving parents in the decision-making process is essential. Parents should be informed about the risks and benefits of NOM, and their consent is necessary for proceeding with this management strategy. In addition, it is important to highlight the necessity of having access to the hospital for ongoing monitoring and subsequent follow-up care.[43,44]

8. Structured Protocols: Utilizing a structured management protocol with clear cut-off criteria for monitoring patient progress can enhance the success of NOM. This includes regular assessments of pain, fever, and laboratory results.[43]

7. Future studies

The implementation of NOMfor acute appendicitis is both safe and feasible in the pediatric population. However, there is a lack of evidence in some aspects of this type of management, so future studies are needed.

Meta-analysis of original studies revealed heterogeneity in results.[32] To determine the effect of age, laboratory, and imaging findings on the success of NOM, more RCTs with similar antibiotic options,

consistent patient inclusion criteria, and follow-up duration are necessary to minimize the heterogeneity.[32,47] Although the parents must be engaged in the decision-making process, it is important to remain aware of the potential selection bias that their involvement may introduce. Hence, minimizing this bias is crucial in future studies.[47] There is a need for additional prospective randomized controlled trials that specifically examine the long-term clinical outcomes associated with this approach, as well as its cost-effectiveness.[21,30,38]

Research indicates that patients with uncomplicated acute appendicitis would benefit from NOM. Identifying the positive response to the nonoperative treatment on the initial evaluation is important. Hence, future studies with a focus on the early differentiation of different forms of appendicitis in children (simple or complicated, progressive or self-limiting) are required to establish gold standard criteria for diagnosis and management.

Conclusion

NOM of acute appendicitis in children has emerged as a considerable alternative to traditional appendectomy, demonstrating a high initial success rate and comparable complication rates between the two treatment strategies. Studies indicate that NOM can avoid surgery in a significant percentage of cases, particularly in patients without appendicoliths or complicated acute appendicitis. Hence, careful patient selection is crucial. While the current evidence supports the safety and efficacy of NOM, further large-scale randomized controlled trials are necessary to solidify its role in clinical practice and to establish clear guidelines for its implementation in pediatric patients with uncomplicated appendicitis.

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