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Non-Operative management of acute appendicitis in children

Çocuklarda akut apandisitin ameliyatsız tedavisi

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Abstract

Purpose: Most studies addressing non-operative management for acute appendicitis have focused on adults, and there are limited data available for children. We aimed to evaluate the results of successful non-operative management in children with acute uncomplicated appendicitis with our "additional criteria" and find which factors could be affecting the success rate and which cases could be candidates for non-operative management.

Materials and methods: A total of 26 patients who were diagnosed with acute uncomplicated appendicitis and received non-operative management were re-evaluated retrospectively. Defining uncomplicated appendicitis was based on the duration of symptoms (<24 hours), clinical history, and radiologic findings. The radiologic evaluation was based on ultrasonography and computed tomography. The patients received an intravenous antibiotic combination (sulbactam/ampicillin, gentamicin, clindamycin) for five days at the hospital; the treatment was completed after 10 days with an oral antibiotic combination (amoxicillin/clavulanate, metronidazole). The cases have a follow-up period of up to two years.

Results: The mean patient age and follow-up time were 10.42±3.65 years and 30.15±5 months, respectively. The mean leukocyte count, C-reactive protein (CRP), and appendix diameter values were 15.82±5.4×109/L, 20.38±33.4mg/dL, and 7.87±1.4 mm on admission. None of the patients had an early failure, complication, or adverse event. Recurrent appendicitis occurred in only one case (4%) that was treated by laparoscopic appendectomy during the follow-up.

Conclusion: Non-operative management for acute uncomplicated appendicitis in children regarding long-term outcomes with our criteria was satisfactory and initial success rates were excellent.

Keywords: Acute appendicitis, appendectomy, children, conservative treatment, non-operative management.

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Öz

Amaç: Akut apandisit için ameliyatsız tedaviyi ele alan çoğu çalışma yetişkinlere odaklanmıştır ve çocuklar için sınırlı veri mevcuttur. Akut komplikasyonsuz apandisitli çocuklarda başarılı ameliyatsız yönetimin sonuçlarını "ek kriterlerimiz" ile değerlendirmeyi ve hangi faktörlerin başarı oranını etkileyebileceğini ve hangi vakaların ameliyatsız tedaviye aday olabileceğini bulmayı amaçladık.

Gereç ve yöntem: Akut komplikasyonsuz apandisit tanısı alan ve ameliyatsız tedavi uygulanan toplam 26 hasta retrospektif olarak yeniden değerlendirildi. Komplike olmayan apandisit tanımlaması semptomların süresine (<24 saat), klinik öyküye ve radyolojik bulgulara dayanıyordu. Radyolojik değerlendirme ultrasonografi ve bilgisayarlı tomografi ile yapıldı. Hastalara hastanede beş gün intravenöz antibiyotik kombinasyonu (sulbaktam/ampisilin, gentamisin, klindamisin) verildi; tedavi oral antibiyotik kombinasyonu (amoksisilin/klavulanat, metronidazol) ile 10 güne tamamlandı. Olguların ortalama takip süresi iki yıldı.

Bulgular: Ortalama hasta yaşı ve takip süresi sırasıyla 10,42±3,65 yıl ve 30,15±5 aydı. Başvuru anındaki ortalama lökosit sayısı, C-reaktif protein (CRP) ve apendiks çapı değerleri 15,82±5,4×109/L, 20,38±33,4mg/dL ve 7,87±1,4 mm idi. Hastaların hiçbirinde erken başarısızlık, komplikasyon veya yan etki görülmedi. İzlemde sadece bir olguda (%4) tekrarlayan apandisit gelişti ve laparoskopik apendektomi ile tedavi edildi.

Sonuç: Çocuklarda akut komplike olmayan apandisitin ameliyatsız yönetimi, kriterlerimize göre uzun vadeli sonuçlara göre tatmin ediciydi ve başlangıç başarı oranları mükemmeldi.

Anahtar kelimeler: Akut apandisit, appendektomi, çocuk, konservatif tedavi, ameliyatsız tedavi.

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Introduction

The most frequent abdominal surgical pathology in children is acute appendicitis [1]. The standard therapy for acute appendicitis in children is appendectomy. Surgical intervention has some complications that can result in morbidity and mortality [2]. The surgical approach has been questioned for uncomplicated appendicitis in recent years, and antibiotic therapy has been proposed as an alternative treatment [3]. Non-operative management for acute appendicitis has been developed in adult cases and has been safely adapted for children over time. Only a small number of publications have described non-operative treatment among children [4-16]. Specific criteria and various results were used in these research. This study aimed to evaluate non-operative management for uncomplicated cases and find which factors could be affecting success rate and outcomes.

Materials and methods

This study was retrospective and descriptive. After obtaining permission from the Pamukkale University Non-Interventional Clinical Research Ethical Committee, the records of 180 cases diagnosed with acute appendicitis from February 2019 to February 2020 were reviewed. A total of 154 out of 180 patients were managed surgically (77 open appendectomies and 77 laparoscopic appendectomies), and the rest (26 patients) were treated non-operatively. Of the non-operatively treated appendicitis cases, only those who completed their two-year follow-up were included in the study. Patients with complicated appendicitis, fever at the time of admission, signs of fecalith on radiologic evaluation, and a follow-up period of less than two years were excluded from the study.

Diagnosis of acute appendicitis

The diagnosis of acute appendicitis was based on history, physical examination, laboratory results, and radiologic evaluation. Radiologic scans were routinely used in suspected acute appendicitis cases. Ultrasound (US) is preferred as the first-choice imaging method. However, a CT scan was used when the appendix could not be seen on an ultrasonographic exam. The appendix diameter was higher than 6 mm, uncompressible appendix, and echogenicity of tissue around the appendix were confirmed as acute appendicitis in the ultrasonographic exam.

Definitions

Our inclusion criteria for non-operative management were defined as symptom duration of less than 24 hours, localized tenderness, no signs of fecalith on radiologic evaluation, and no fever at the time of admission (Table 1). The symptom duration of longer than 24 hours, generalized tenderness on physical exam, and radiologically suspected complicated appendicitis cases (abscess, phlegmon, irregular appendix wall) were managed operatively.

Table 1. Patient evaluation and inclusion criteria for non-operetive management

Patient evaluation	Inclusion criteria for non-operative management
Symptom duration	<24 hours
Clinical history	No fever and no additional disease
Physical examination	Localized tenderness
Radiologic evaluation (Ultrasonography and CT)	Without fecalith and perforation

Treatment protocol

The non-operative management option was applied to those who did meet the criteria for non-operative management. Oral intake was not permitted during the first 24 hours of antibiotic treatment and hydration was provided by intravenous (IV) crystalloid solutions. The IV antibiotic protocol was ampicillin-sulbactam (150 mg/kg/day, divided into four doses), gentamicin (5 mg/kg/day, divided into two doses), and clindamycin (40 mg/kg/day, divided into four doses). All cases were evaluated by a physical examination at 12-hour intervals. For the patients who responded to antibiotic treatment after 24 hours, oral feeding was initiated. IV antibiotic duration was five days in all cases at

the hospital, and all patients were discharged from the clinic with an oral antibiotic regimen (amoxicillin/clavulanic acid and metronidazole). Total antibiotic duration (IV and oral) lasted for 10 days.

Follow-up

All cases were re-evaluated by laboratory investigation and radiological examination. All of the patients were re-evaluated only by a physical exam on the second and seventh days of discharge at the outpatient clinic. Additional radiologic and laboratory screenings were not repeated at the outpatient clinic.

All procedures carried out during this study complied with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards, as well as the ethical norms of the institutional and/or national research committee. The parents were informed about the treatment protocol and complications.

Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 22.0 (IBM Corp, Armonk, NY). Statistics are presented as weighted mean ± standard deviation. The Kolmogorov-Smirnov test was performed to assess normal distribution. Parametric variables were analyzed by independent t-test and non-parametric variables by Mann-Whitney U test. The homogeneity of variance was determined by Levene's test. The level of statistical significance for descriptive statistics was set at $p<0.05$.

Results

The mean patient age was 10.42±3.6 years (range: 5-17 years). A total of 12 (46%) cases were males and 14 (54%) were females; the male-to-female ratio was 0.75. The follow-up period of the cases ranged from 24 to 37 months, and the mean follow-up time was 30.15±5 months.

Initial white blood cell (WBC) and C-reactive protein (CRP) levels at admission were 15.82±5.4×10^9/L and 20.38±33.4mg/dL, respectively. All cases were evaluated by the abdominal US at admission. The main criteria of non-operative management of acute appendicitis was no signs of fecaliths in the appendix lumen; therefore, most cases were evaluated by a CT scan. If signs of fecalith were not clearly reported in the US exam, they were evaluated by a CT scan. Neither unresponsive cases nor complications (e.g. sepsis, ileus, perforation, and adverse drug events) were observed during the antibiotic treatment. Initial success rates were 100%. Readmission to the hospital was observed in one case at the 20th month of post-non-operative treatments, and they were subsequently treated laparoscopically. Histopathologic evaluations have revealed that no perforation signs were recorded in the specimen.

Discussion

Pediatric appendicitis has a high perforation rate, and removal of the appendix is a conventional surgical operation. Therefore, appendectomy is the first choice of treatment in children. However, surgical interventions and general anesthesia have some inevitable complications (e.g. bleeding, ileus, surgical site infection, and pneumonia). For these reasons, in recent years, non-operative management has been preferred in some cases of acute appendicitis [17]. The basic hypothesis is that other acute appendicitis-like conditions (e.g. uncomplicated diverticulitis, salpingitis, and necrotizing enterocolitis) regress with antibiotics with a high success rate, especially when the medical treatment is started early [18]. Few studies have addressed non-operative management for acute appendicitis among pediatric patients, while this is a well-known option in the adult patient population [19].

Previous studies have demonstrated widely different success rates. These varied results might be due to patient selection criteria and antibiotic therapy protocols [2, 4-16]. Antibiotic selection, antibiotic duration, and time for IV/per oral route have also been attracting research interest. A varied ratio of overall success is presented in the literature by the studies regarding children being managed non-operatively. The overall success rate in our study is higher than many studies in the literature. Among those studies, it is seen that the overall success rate was higher in studies where the patients were with short symptom duration (<36 hours) [4, 14, 15].

In this study, we reduced the symptom duration between the onset of complaints and admission (<24 hours), and we required

additional criteria such as the patients to be “fever-free” at the initial examination. Being fever-free at the time of admission is an important sign of a non-complicated inflammatory period. This approach provided early antibiotic initiation and suppressed the inflammatory process. To date, meta-analyses are demonstrating that being fever-free at the time of admission is not an inclusion criterion for non-operative management [20, 21]. Similarly, early antibiotic initiation has been reported to cause low recurrence rates of non-operative treatment [4, 14, 15].

The inclusion and exclusion criteria for non-operative management have been determined with/without fecalith and appendix diameter in imaging studies [4, 7-9, 14, 15]. One of the main criteria in our study was no signs of fecaliths in the appendix. Unlike in previous studies, we performed a CT scan in 16 (61.5%) of the cases in our series. This is because, in the US examination, only 6 (23%) appendices were detected and verified without fecalith in the imaging studies. CT scan has high sensitivity and specificity rate for the diagnosis of acute appendicitis; however, the routine usage of CT scan is not recommended due to the high radiation exposure. The reduction of ionizing radiation has provoked the increased usage rate of CT year on year [22, 23]. Sometimes CT scanning may be the first choice of radiologic evaluation for undiagnosed patients and obese children. The usage rates of CT imaging for the diagnosis of acute appendicitis vary according to clinical practice, surgeon preference, and institutions. The average rate is reported as 30-40% [24-26].

In some studies, to decide on non-operative management, the appendix diameter has been taken into consideration. It has been reported that the appendix diameter should be ≤9, ≤10, and ≤11 mm in various studies [7, 9, 15, 27]. In the current study findings, we did not consider appendix diameter. In contrast, the appendix diameter was found higher than 8 mm in 9 (34%) patients, and they were treated non-operatively. However, the cut-off value of appendix diameter for non-operative management remains controversial. A critical evaluation was that acute uncomplicated appendicitis is suppressed with antibiotics.

The selection of antibiotics (e.g. cephalosporin, carbapenem, and β-lactam) and the duration of the prescription/therapy might differ among the clinical series [4-16]. Antibiotic duration for IV and oral administration has been reported to vary in the earlier reports. In our series, we preferred triple and narrow-spectrum antibiotics by IV route administered in the hospital for five days. The duration of antibiotic therapy was longer than the other reported series. Even in the early responding treatments of cases, IV treatment was completed in five days, as reported earlier.

Perez Otero et al. reported that the antibiotic treatment was first applied in the emergency department and was provided to be used at home for two or three days in the total course. The same analyses have reported that the success rate of their treatment was 58-99%. In our study, the positive responses of all cases to the treatment might be a result of the long-term usage of antibiotics.

The case numbers and follow-up periods of the literature studies were evaluated similarly. For long-term results, follow-up periods between six months and 4.3 years were reported. Besides, it has long been established that recurrences are the main factor in the success rate in the follow-up period. The early failure rate of these studies was between 1.2% and 41.6%, and the long-term failure rate was 8-42% in children [2, 4-16, 20]. There was no early failure case in our study; however, the long-term failure rate was 9% due to five recurrences of appendicitis. A meta-analysis of previous studies reported that the rate of appendectomy due to recurrence appendicitis was 18-42% within a one-year follow-up period [27-30]. Therefore, we included cases that have a follow-up period of at least two years. The mean follow-up period was 30 months in our study, whereas a small number of studies had a longer follow-up period than ours.

The primary limitations of this study were its retrospective, uncontrolled, single-center design. Another limitation of our study is the longer duration of IV antibiotic therapy (five days) in the hospital. However, this can be interpreted as the learning curve of our clinic. In our current practice, we hospitalize patients for two or three days for IV antibiotic therapy.

In conclusion, in this observational study, we found that non-operative management in children for acute uncomplicated appendicitis in selected cases is a safe and effective treatment method. Based on our findings, we propose that the success rate of non-operative management for clinically and radiologically proven acute appendicitis cases could be improved by applying two significant treatment criteria, i.e, less than 24 hours of symptom duration and fever-free at the time of admission.

Conflict of interest: No conflict of interest was declared by the authors.

References

1. Ashcraft KW, Holcomb GW, Murphy JP, et al, eds. Ashcraft's pediatric surgery. 6th ed. London: Saunders/ Elsevier; 2014
2. Scott A, Lee SL, DeUgarte DA, Shew SB, Dunn JCY, Shekherdimian S. Nonoperative Management of Appendicitis. Clin Pediatr (Phila) 2018;57:200-204. https://doi.org/10.1177/0009922817696465
3. Svensson JF, Hall NJ, Eaton S, Pierro A, Wester T. A review of conservative treatment of acute appendicitis. Eur J Pediatr Surg 2012;22:185-194. https://doi.org/10.1055/s-0032-1320014
4. Abeş M, Petik B, Kazil S. Nonoperative treatment of acute appendicitis in children. J Pediatr Surg 2007;42:1439-1442. https://doi.org/10.1016/j.jpedsurg.2007.03.049
5. Armstrong J, Merritt N, Jones S, Scott L, Bütter A. Non-operative management of early, acute appendicitis in children: is it safe and effective? J Pediatr Surg 2014;49:782-785. https://doi.org/10.1016/j.jpedsurg.2014.02.071
6. Koike Y, Uchida K, Matsushita K, et al. Intraluminal appendiceal fluid is a predictive factor for recurrent appendicitis after initial successful non-operative management of uncomplicated appendicitis in pediatric patients. J Pediatr Surg 2014;49:1116-1121. https://doi.org/10.1016/j.jpedsurg.2014.01.003
7. Steiner Z, Buklan G, Stackievicz R. A role for conservative antibiotic treatment in early appendicitis in children. J Pediatr Surg 2015;50:1566-1568. https://doi.org/10.1016/j.jpedsurg.2015.04.008
8. Gorter RR, van der Lee JH, Cense HA, et al. Initial antibiotic treatment for acute simple appendicitis in children is safe: short-term results from a multicenter, prospective cohort study. Surgery 2015;157:916-923. https://doi.org/10.1016/j.surg.2015.01.008
9. Minneci PC, Mahida JB, Lodwick DL, et al. Effectiveness of patient choice in nonoperative vs surgical management of pediatric uncomplicated acute appendicitis. JAMA Surg 2015;151:408-415. https://doi.org/10.1001/jamasurg.2015.4534
10. Tanaka Y, Uchida H, Kawashima H, et al. Long-term outcomes of operative versus nonoperative treatment for uncomplicated appendicitis. J Pediatr Surg 2015;50:1893-1897. https://doi.org/10.1016/j.jpedsurg.2015.07.008
11. Svensson JF, Patkova B, Almström M, et al. Nonoperative treatment with antibiotics versus surgery for acute nonperforated appendicitis in children: a pilot randomized controlled trial. Ann Surg 2015;261:67-71. https://doi.org/10.1097/sla.0000000000000835
12. Hartwich J, Luks FI, Watson Smith D, et al. Nonoperative treatment of acute appendicitis in children: A feasibility study. J Pediatr Surg 2016;51:111-116. https://doi.org/10.1016/j.jpedsurg.2015.10.024
13. Caruso AM, Pane A, Garau R, et al. Acute appendicitis in children: not only surgical treatment. J Pediatr Surg 2017;52:444-448. https://doi.org/10.1016/j.jpedsurg.2016.08.007
14. Steiner Z, Buklan G, Stackievicz R, et al. Conservative treatment in uncomplicated acute appendicitis: reassessment of practice safety. Eur J Pediatr 2017;176:521-527. https://doi.org/10.1007/s00431-017-2867-2
15. Steiner Z, Buklan G, Gutermacher M, Litmanovitz I, Landa T, Arnon S. Conservative antibiotic treatment for acute uncomplicated appendicitis is feasible. Pediatr Surg Int 2018;34:283-288. https://doi.org/10.1007/s00383-018-4226-4
16. Mudri M, Coriolano K, Bütter A. Cost analysis of nonoperative management of acute appendicitis in children. J Pediatr Surg 2017;52:791-794. https://doi.org/10.1016/j.jpedsurg.2017.01.050
17. Rentea RM, St Peter SD. Contemporary management of appendicitis in children. Adv Pediatr 2017;64:225-251. https://doi.org/10.1016/j.yapd.2017.03.008
18. Rentea RM, Peter SDS, Snyder CL. Pediatric appendicitis: state of the art review. Pediatr Surg Int 2017;33:269-283. https://doi.org/10.1007/s00383-016-3990-2
19. Styrud J, Eriksson S, Nilsson I, et al. Appendectomy versus antibiotic treatment in acute appendicitis. A prospective multicenter randomized controlled trial. World J Surg 2006;30:1033-1037. https://doi.org/10.1007/s00268-005-0304-6

20. Maita S, Andersson B, Svensson JF, Wester T. Nonoperative treatment for nonperforated appendicitis in children: a systematic review and meta-analysis. Pediatr Surg Int 2020;36:261-269. https://doi.org/10.1007/s00383-019-04610-1
21. Mosuka EM, Thilakarathne KN, Mansuri NM, et al. A systematic review comparing nonoperative management to appendectomy for uncomplicated appendicitis in children. Cureus 2021;19;13:e18901. https://doi.org/10.7759/cureus.18901
22. Glass CC, Rangel SJ. Overview and diagnosis of acute appendicitis in children. Semin Pediatr Surg 2016;25:198-203. https://doi.org/10.1053/j.sempedsurg.2016.05.001
23. Partrick DA, Janik JE, Janik JS, Bensard DD, Karrer FM. Increased CT scan utilization does not improve the diagnostic accuracy of appendicitis in children. J Pediatr Surg 2003;38:659-62. https://doi.org/10.1016/jpsu.2003.5017
24. Glass CC, Saito JM, Sidhwa F, et al. Diagnostic imaging practices for children with suspected appendicitis evaluated at definitive care hospitals and their associated referral centers. J Pediatr Surg 2016;51:912-916. https://doi.org/10.1016/j.jpedsurg.2016.02.055
25. Kotagal M, Richards MK, Chapman T, et al. Improving ultrasound quality to reduce computed tomography use in pediatric appendicitis: the Safe and Sound campaign. Am J Surg 2015;209:896-900. https://doi.org/10.1016/j.amjsurg.2014.12.029
26. Perez Otero S, Metzger JW, Choi BH, et al. It's time to deconstruct treatment-failure: a randomized controlled trial of nonoperative management of uncomplicated pediatric appendicitis with antibiotics alone. J Pediatr Surg 2022;57:56-62. https://doi.org/10.1016/j.jpedsurg.2021.09.024
27. Bachur RG, Lipsett SC, Monuteaux MC. Outcomes of nonoperative management of uncomplicated appendicitis. Pediatrics 2017;140:20170048. https://doi.org/10.1542/peds.2017-0048
28. Georgiou R, Eaton S, Stanton MP, Pierro A, Hall NJ. Efficacy and safety of nonoperative treatment for acute appendicitis: a meta-analysis. Pediatrics 2017;139:e20163003. https://doi.org/10.1542/peds.2016-3003
29. Gorter RR, The SML, Gorter Stam MAW, et al. Systematic review of nonoperative versus operative treatment of uncomplicated appendicitis. J Pediatr Surg 2017;52:1219-1227. https://doi.org/10.1016/j.jpedsurg.2017.04.005
30. Kessler U, Mosbahi S, Walker B, et al. Conservative treatment versus surgery for uncomplicated appendicitis in children: a systematic review and meta-analysis. Arch Dis Child 2017;102:1118-1124. https://doi.org/10.1136/archdischild-2017-313127

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Authors' contributions to the article

O.U. constructed the main idea and hypothesis of the study. O.U. developed the theory and arranged/edited the material and method section. O.U. and I.G.A. have done the evaluation of the data in the Results section. Discussion section of the article written by O.U.

O.U. and I.G.A. reviewed, corrected and approved. In addition, all authors discussed the entire study and approved the final version.