Original Research Article

Conservative Management of Uncomplicated Acute - Appendicitis in Children

ABSTRACT

objective To evaluate the safety and outcome of conservative treatment of uncomplicated acute appendicitis in children. Our main outcomes were: The response to conservative treatment, complications during the course of this treatment and short term recurrence of appendicitis in initial responders to treatment.

Methods we used antibiotics instead of surgery to treat 100 children aged 4-18 years who were diagnosed with acute uncomplicated appendicitis (AUA) using Pediatric Appendicitis Score (PAS score).

Results The success rate of NOM in our series was 84%. Most cases showed improvement of both clinical & laboratory findings on 2nd day of management. While 16% failed NOM and operated with laparoscopy. We followed up our cases who had successful NOM for any relapse at one week, 6weeks, 3months then 6months. Readmission for cases who had a relapse occurred in 4 cases, one case relapsed after 6 weeks of discharge, patient failed conservative treatment and was operated laparoscopy. Another 2 cases were readmitted with a relapse after 3 months and one case after 6 months. They were managed conservatively again, and responded to NOM. The relapse failure rate was 4.7%.

conclusion Using conservative management of AUA among children aged 4-18 years, proved to be safe, effective and have a low rate of complications. It reduced the negative appendectomy rate to 1%. It is associated with a low relapse rate within 6 months and significantly reduces the treatment cost. With parents counseling, the parents can accept the NOM and had their fear alleviated.

1. INTRODUCTION

Appendectomy is considered the gold standard treatment for acute appendicitis by most surgeons either open or laparoscopic. However, an alternative approach to treat acute uncomplicated appendicitis in children with antibiotics and without an appendectomy has established a tremendous momentum in the past few years. [1, 2]

Despite both open and laparoscopic appendectomy being regarded as low-risk and effective procedures, operative management may still associated with risks or complications. These risks may be associated with general anesthesia or surgical complications such as hemorrhage, surgical site infection, injury to surrounding structures, ileus, adhesive small bowel obstruction or the potential need for reoperation.[3]

While nonoperative treatment strategy can avoid these troubles, it requires strict observation of patients to reduce the probability of occurrence or progression of the course of acute uncomplicated appendicitis. [4]

There has been an increased interest in the conservative management of appendicitis over the last 20 years. The main benefit of nonoperative treatment is that it avoids the difficulties of surgery and the risk of anesthesia. Additionally, the successful use of antibiotics in treating intra-abdominal infections such as diverticulitis has aroused renewed interest in the nonoperative management of appendicitis. [5]

2. PATIENTS AND METHODS

This prospective study was conducted on children from 4 to 18 years with acute right lower quadrant pain, with a diagnosis of uncomplicated acute appendicitis who were managed at the Pediatric Surgery Unit, Tanta University Hospitals in the period between Feb 2021 till Feb 2022. We included children with PAS ≥ 7 with or without positive USS for acute appendicitis and children with PAS: 4-6 with positive USS for acute appendicitis. We excluded Children with, evidence of complicated appendicitis, Cognitive disability, Immune compromised, chronic abdominal pain or those previously treated conservatively from suspected appendicitis, PAS ≤ 3, PAS 4−6 with negative USS.

Evaluation of children was done using clinical assessment using PAS score, laboratory investigations (TLC), CRP), imaging studies : US and CT when needed,

Conservative treatment:

Patients were assigned for conservative treatment if their score is ≥ 7, with or without positive USS for acute appendicitis or those with a score of 4−6 with positive USS for appendicitis. This conservative treatment consists of: 1. Nothing per mouth (NPO). 2. IV Fluids : according to age and weight we may us (Holliday- segar method) [(6)] 3. Parentral Third generation cephalosporins in a dose of 100 mg/kg BW/day in two divided doses. 4. Parentral metronidazole in adose of 7. 5mg/kg every 8h. 5. Analgesics are used as required to control pain on a dose / weight basis, starting with paracetamol and adding NSAIDs if needed. 6. Once the child is well clinically and tolerating oral intake, antibiotics are continued with oral third generation cephalosporins (suprax 8mg/kg/day in oral suspension, 400 mg/day chewable tablets in children weighing more than 45kg or older than 12years and oral metronidazole 30 mg/kg in three divided doses for 5 days.

At least twice daily follow up of temperature, pulse rate, course of pain and abdominal examination, daily Total & differential leucocytic count and CRP, USS re-examination after 48h from admission, if the ultrasound was again non-diagnostic or diagnostic for simple appendicitis, patients remained in the group of “conservative treatment”.

Persistence or deterioration of symptoms and signs of appendicitis for at least 3 days is an indication of appendectomy either open or laparoscopic according to available resources. Any complications during the course of treatment were reported. The resected appendix was sent for histopathology. Patients were discharged after improvement of clinical and laboratory data on 5 days course of oral antibiotics. They were

instructed about alarming symptoms that may need readmission or surgical intervention.

Follow up: First follow-up visit was planned at one week after hospital discharge then at 6 weeks, 3 months and 6 months, in the outpatient clinic. During the 1st 2 follow up visits patients were evaluated clinically. Laboratory or imaging investigations were ordered when needed. Any relapses or readmission were reported.

3. Results :

Our study included 100 patients with acute uncomplicated appendicitis managed in the Pediatric Surgery Unit, Tanta University Hospitals during the period from 1st of 2021 till the 1st of Feb 2022. Their age ranged from 4 to 18 years, 52 % of them were males and 48 % were females.

Analysis of the incidence of symptoms & signs showed that nausea was presented in 80 children (65 of successful NOM group and 15 of failed NOM group, vomiting was presented in 57 children (47 of successful NOM group and 10 of failed NOM group), anorexia in 78 (65 of successful NOM group and 13 of failed NOM group), 95 had tender MacBurny point on percussion (79 of successful NOM group (94%) and 16 of failed NOM group (100%)), 79 had cough tenderness (64 of successful NOM group (76%) and 15 of failed NOM group (93.8%)), 49 have fever ≥ 38 (35 of successful NOM group (41.7%) and 14 of failed NOM group(87.5%), with minimum duration of symptoms one day and maximum 7 days (mean 2.5-3 days), Migration of pain was found in 61 (46 of successful NOM group (54.8%) and 15 of failed NOM group (93.8%).

As regarding laboratore data, Leucocytic count more than 11000 was found in 54 (41 of successful NOM group (48.8%) and 13 of failed NOM group (81.3%). there was gradual return of leucocytic count back to normal values within two days of NOM. While, As regarding CRP, 20 patients at admission had normal CRP count, all of them managed conservatively while 80 had count more than 6 (64 of Successful NOM group and all patients of Failed NOM group. Gradual improvement and decrease of CRP ratio in studied patients especially Successful NOM group while 4 patients of Failed NOM group showed improvement of CRP count without improved clinical signs.

According to US findings in our patients on admission, there was no US signs of AA in 2 patient and 72 patients were showing signs of AA (56 of successful NOM group and 16 of failed NOM group), while a rim of intraperitonial free fluid with mesenteric lymphadenitis was found in 26. On follow up US after 48 h no signs of appendicitis were found in 60 children, 20 children showing signs of appendicitis while 20 children were showing rim of FF + multiple enlarged mesenteric lymphadenitis.

According to PAS score calculation we found that on day zero (admission day) 19 children had score 4-6 with US signs of AA and 81 had score 7-10 (65 of successful NOM group and 16 of failed NOM group) with or without US signs of AA with total positive us signs in 56 patient. With follow up of clinical date we found that by the fourth day of NOM Eighty four children improved with a PAS score of 3 or less and were discharged as successful NOM group, Fourteen children had score 7-10, failed conservative management and 13 of them

were operated laparoscopy & one case was operated by open surgery.

Histopathological examination of the removed appendix in the operated cases, showed that one case had a normal appendix, 5 had acute catarrhal appendicitis, while 10 had acute suppurative appendicitis.

As regard follow uo and relapse rate:

During the first week of follow up period, no cases were readmitted because of recurrent abdominal symptoms. During the next 6 weeks, one case was readmitted and failed to respond to NOM for three days and operated laparoscopic. In the next 3months two cases were admitted for 3 days and responded to NOM. In the next 6months, one case was admitted also for 3days and responded to NOM.

According to validity (sensitivity, specificity) for total PAS to discriminate operated patients from conservative patients, we found that sensitivity of total PAS was 81.25, specificity was 76.19.

4. Discussion:

The diagnosis of pediatric AA remains challenging. Some clinical scores are evolved to help diagnosis of AA. They mainly depend on 1- good history taking, 2- physical examination, 3- laboratory findings (TLC, CRP). The ideal clinical score could accurately distinguish between patients who need immediate operative care and patients who may be postponed to have further investigation or observation. [7]

PAS is commonly used in children. Children with suspected AA were stratified into low risk group (score < 3), intermediate risk (score 4-6) and high risk (score 7-10). [8]

The traditional treatment of AA is either conventional open or laparoscopic appendectomy. However, some reports claimed that cases of Discussion & &56& acute uncomplicated appendicitis (AUA) may be conservatively managed using only antibiotics and analgesia with rest of gastrointestinal tract if needed. [7]

Minneci et al showed that children with successful NOM had fewer disability days and returned to school more quickly. They concluded that NOM is safe and maintains a good quality of life. [9]

While planning for NOM most parents in our study were convinced with this line of treatment. Some parents were initially afraid and hesitated due to the myth of rupture of the appendix. We explained them all the steps of NOM including the advantages and disadvantages. High lighting the meticulous observation, while would detect any deterioration or non-response at an early stage before complications develop. At the end parents were convinced and accepted the plan of NOM. None of the parents of cases were rushed to have an appendectomy. They were satisfied with the results especially those who had successful NOM.

During our series we performed only 16 laparoscopic appendectomies out of 100 patients. They passed smooth without any operative or postoperative complications. While children who underwent NOM (84 %) returned to normal activities after a mean of 5 days.

Georgiou et al., reported a success rate of NOM in 97% of all included children. There was no statistical significance of the rate of complications in both NOM group and failed NOM group. [10]

Our study included 100 children aged 4-18 years as at this age children start to communicate well and can express his feelings, diagnosed with AUA. They were diagnosed using PAS, pelvic-abdominal ultrasound and CRP levels. According to interpretation of PAS we excluded patients with PAS ≤ 3. We included children whose PAS is 7-10. The children whose PAS was 4-6 (gray zone) were included if their ultrasound report showed positive findings of AUA.

Lee et al. included 51 children aged 3–17 years. Their PAS Score was ≥6. They excluded patients with symptoms ≥ 5 days, pregnant patients, immunodeficient patients, patients with diffuse peritonitis, or an abscess >5 cm or perforation. [(11)]

Steiner et al. Included 362 children aged 3–16. Their PAS Score was ≥7. They excluded cases that had duration of symptoms ≥36 h, diffuse peritonitis, an appendicolith, an appendiceal diameter ≥10 mm, and cases presented with an abscess. [(12)]

Children with PAS score ≥ 4 were the main zone of our study and confirmed diagnosis with US. All of operated cases were scored more than 7 while, patients who had score 4-6 were a gray zone and needed US to confirm diagnosis all of them improved with NOM. We changed our trend after completing the study by managing those children at home, while children with score 7-10 need admission and close follow up.

In our study the mean duration of symptoms was 2.5 days in children who had successful NOM. While it was 3.5 days in patients who failed NOM. However, there was no statistical significance.

Isani et al., reported that the success of NOM was not affected by the duration of symptoms whether > or < 4 days. Moreover, the duration of

symptoms didn't relate to the readmission rate, hospital stay or the development of complications. [13]

In our series NOM depended mainly on intravenous (IV) 3rd generation cephalosporin in a dose of 100 mg/kg BW/day in two divided doses and metronidazole in a dose of 7.5mg/kg every 8h. Shifting to oral 3rd generation cephalosporin and oral metronidazole at home for 5 days after discharge.

While in two studies by Lee et al, Steiner et al depended on IV ceftriaxone and metronidazole or ciprofloxacin and metronidazole during conservative management. They Discussion & &60& followed their patients at home on oral amoxicillin/ clavulanic acid or ciprofloxacin and metronidazole or cefdinir and metronidazole for 10 days. [11, 12]

Minneci et al. prescribed IV piperacillin / tazobactam or ciprofloxacin and metronidazole for their patients for 3 or 4 days of hospital stay. Then oral amoxicillin/ clavulanic acid or ciprofloxacin and metronidazole to complete10 days.[14] Svensson et al. used IV meropenem and metronidazole regimen in hospital at for at least 2 days. As soon as the children were tolerating oral intake, they were given oral ciprofloxacin and metronidazole for a total of 10 days treatment. [15]

In our study analgesics were prescribed according to severity of pain, starting with paracetamol. If there was still pain a non-steroidal antiinflammatory analgesic (e.g. ketorolak) was added. We didn't need opioid analgesics in any patient.

Lee et al, Steiner et al used analgesia with their patients when needed, they used non-steroidal anti-inflammatory drugs. [11, 12]

In our study oral intake was restricted only in patients who had sever GIT symptoms such as vomiting, abdominal colics and anorexia. Once

the patient can tolerate oral intake, feeding was gradually introduced. Starting with fluids then semi solids and full oral feeding before or after discharge.

In Lee et al and Steiner et al studies oral intake was restricted for at least 48h. Once patient tolerated shifting to oral intake and oral antibiotics. [11, 12]

Svensson et al, Minneci et al restricted oral intake during the first 24h of the management. They discharged patients when they became afebrile for at least 24h, abdominal pain free, and tolerated oral intake. [14, 15]

During NOM, we stressed on frequent examination and meticulous observation of patients, daily LC & CRP were performed; all to detect any deterioration or complication early. NOM was practiced for a maximum 3 days, if patients didn`t improve within three days, or deterioration occurred before that time limit, we decided to operate. The clinical examination laboratory investigation and abdominal US imaging were repeated on every clinic visit during the follow up period in cases who responded to NOM.

The mean duration of hospital stay in our study in patients who had successful NOM was 2.5 days while hospital stay in patients who had failed conservative management was 3.5 days.

Max Knaapen et al reported that the median duration for hospital stay was 2.5 days under observation with daily monitoring of patients. Appendectomy was decided once there was deterioration of symptoms and signs. [16]

While In Jeff Armstrong et al study the mean duration of hospital stay in patients who success NOM was 1.5 days while in operated patients was 1.3 days. [17] , and In Minneci et al, study the mean duration

of hospital stay was 37 h in NOM group also it was 20 h in operated group. [15]

In our study we had a high initial success rate of NOM of 84% and a low relapse & readmission rate within 1 year of 4.7 %.

In a meta-analysis of randomized controlled trials including 5 studies and 1430 patients with uncomplicated acute appendicitis, the success rate of NOM during the initial hospitalization was 84%. Readmission for recurrent appendicitis requiring treatment occurred in another 21% of patients during the subsequent year of follow-up. Overall, treatment with antibiotics was associated with a 39% risk reduction in complications compared with those undergoing appendectomy. The main drawback of this meta-analysis study was inclusion of adult patients only. [18]

We operated 16% of patients after failure of conservative management with laparoscopy except one case with conventional way. One patient of 84 patients was readmitted after 6weeks during the follow up period and operated with laparoscopy. Histopathological examination of resected appendix revealed that no signs of inflammation was found in one case while, 5 cases showed acute on top of chronic appendicitis and 10 cases with suppurative appendicitis.

A cording to total cost in our series, there was a higher cost of operated cases than NOM patients. The median cost in NOM children was 1850.0 (1150.0 – 2500), while that of operated cases was 4000.0 LE (3700.0 – 4500.0).

The randomized trial of Sippola et al revealed that the overall costs were 1-6 times higher in the children subjected to appendectomy when compared with children who had successful NOM. [19]

5. conclusion:

Using conservative management of AUA among children aged 4-16 years, proved to be safe, effective and have a low rate of complications. It reduced the negative appendectomy rate to 1%. It is associated with a low relapse rate within 6 months and significantly reduces the treatment cost. With parents counseling, the parents can accept the NOM and had their fear alleviated.

However a controlled randomized trial on a bigger number of cases is needed to validate these results.

Reference:

1. Hutchings N, Wood W, Reading I, et al. Contract Studey -Conservative Treatment of Appendicitis in Children (feasibility): study protocol for a randomised controlled Trial. Trials 2018 ;1 9(1):153.
2. Ramon R, Sarah M, Marguerite A, et al. Systematic review of nonoperative versus operative treatment of uncomplicated appendicitis. j Ped Surg . 2017;04: 005. 0022 _3468.
3. Varadhan KK, Neal KR, Lobo DN, et al. Safety and efficacy of antibiotics compared with appendicectomy for treatment of uncomplicated acute appendicitis: meta-analysis of randomised controlled trials. B M J. 2012;344:e2156.
4. Kessler U, Mosbahi S, Walker B, et al. Conservative treatment versus surgery for uncomplicated appendicitis in children: a References & &69& systematic review and meta-analysis. Arch Dis Child 2017; 102:1118–1124.
5. 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(5):916-923.
6. Cavari Y, Pitfield AF, Kissoon N. Intravenous maintenance fluids revisited. Pediatr Emerg Care. 2013;29(11):1225-8.
7. Schneider C, Kharbanda A, Bachur R. Evaluating appendicitis scoring systems using a prospective pediatric cohort. Ann Emerg Med. 2007;49(6):778-784.e1.
8. Samuel M. Pediatric appendicitis score. J Ped Surg 2002 ;37:877 –881.
9. Minneci PC, Sulkowski JP, Nacion KM, et al. Feasibility of a nonoperative management strategy for uncomplicated acute appendicitis in children. J Am Coll Surg. 2014; 219: 272–279.
10. Georgiou R, Eaton S, Stanton MP, et al. Efficacy and Safety of Nonoperative Treatment for Acute Appendicitis: A Metaanalysis. Pediatrics. 2017;139(3):e20163003.
11. Lee SL, Spence L, Mock K, Wu JX, Yan H, DeUgarte DA. Expanding the inclusion criteria for nonoperative management of uncomplicated appendicitis: outcomes and cost. J Pediatr Surg. 2017;S0022-3468(17):30636–X.
12. 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(3):283–288.
13. Isani MA, Jackson J, Barry WE, et al. Non-Operative Management is More Cost-Effective than Immediate Operation in Perforated Appendicitis Patients with Seven or More Days of Symptoms. J Surg Res. 2019;240:70-79.
14. Minneci PC, Mahida JB, Lodwick DL, et al. Effectiveness of patient choice in nonoperative vs surgical management of pediatric uncomplicated acute appendicitis. JAMA Surg. 2016;151(5): 408–415.
15. 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(1):67–71.
16. Knaapen M, van der Lee JH, Heij HA, van Heurn ELW, Bakx R, Gorter RR. Clinical recovery in children with uncomplicated appendicitis undergoing non-operative treatment: secondary analysis of a prospective cohort study. Eur J Pediatr. 2019;178(2):235-242.
17. 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(5):782-785.
18. Rollins KE, Varadhan KK, Neal KR, Lobo DN. Antibiotics versus appendicectomy for the treatment of uncomplicated acute appendicitis: an updated meta-analysis of randomised controlled trials. World J Surg 2016;40(10):2305-18.
19. S. Sippola, J. Grönroos, R. Tuominen et al. Economic evaluation of antibiotic therapy versus appendicectomy for the treatment of uncomplicated acute appendicitis from the APPAC randomized clinical trial. BJS 2017; 104: 1355–1361.