

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 using pediatric appendicitis score (PAS Score).

RESULTS the success rate of nom in our series was 84%. Most cases showed improvement in both clinical & laboratory findings on 2nd day of management. While 16% failed nom and operated with laparoscopy. We followed up on our cases that had successful nom for any relapse at one week, 6 weeks, 3 months and 6 months. 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 have 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 has 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 parent counseling, the parents can accept the nom and have their fear alleviated.

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 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 be 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 a non-operative 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 non-operative 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 non-operative management of appendicitis. ⁽⁵⁾

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 to 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 use (the Holliday-Segar method) (6) 3). Parenteral third generation cephalosporin in a dose of 100 mg/kg BW/day in two divided doses. 4). Parenteral metronidazole in a dose of 7.5 mg/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 45 kg or older than 12 years 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 leucocytes 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 improving 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 for 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.

UNDER PEER REVIEW

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 in successful NOM group and 15 in failed NOM group, vomiting was presented in 57 children (47 in successful NOM group and 10 in 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 $\geq 38^{\circ}$ C (35 of successful NOM group (41.7%) and 14 of failed NOM group (87.5%)), with a 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 regards laboratory data, a Leucocytes count of more than 11000 was found in 54 (41 of the successful NOM group (48.8%) and 13 of failed NOM group (81.3%)). there was a gradual return of leucocyte count back to normal values within two days of NOM. While, As regards CRP, 20 patients at admission had normal CRP count, all of them managed conservatively while 80 had a count of more than 6 (64 in the successful NOM group) and all patients in Failed NOM group. Gradual improvement and decrease of CRP ratio in studied patients especially in 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 were no US signs of AA in 2 patients and 72 patients were showing signs of AA (56 of successful NOM group and 16 of failed NOM group), while a rim of intraperitoneal 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 the rim of FF + multiple enlarged mesenteric lymphadenitis.

According to the PAS score calculation, we found that on day zero (admission day) 19 children had scores of 4-6 with US signs of AA, and 81 had scored 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 a follow-up of the clinical data, 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 scored 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, and 10 had acute suppurative appendicitis.

As regards follow-up and relapse rate: During the first week of the 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 3 months, two cases were admitted for 3 days and responded to NOM. In the next 6 months, one case was admitted also for 3 days and responded to NOM.

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

Discussion:

The diagnosis of pediatric AA remains challenging. Some clinical scores are evolved to help diagnose AA. They mainly depend on 1- good history taking, 2- physical examination, and 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 the 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 the rest of the gastrointestinal tract if needed. ⁽⁷⁾

Minnecci et al ⁽⁹⁾ 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.

While planning for NOM most parents in our study were convinced of this line of treatment. Some parents were initially afraid and hesitated due to the myth of the rupture of the appendix. We explained to 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. In the end, the 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 smoothly 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 ⁽¹⁰⁾ reported a success rate of NOM in 97% of all included children. There was no statistical significance in the rate of complications in both the NOM group and failed NOM group.

Our study included 100 children aged 4-18 years as at this age children start to communicate well and can express their feelings, diagnosed with AUA. They were diagnosed using PAS, pelvic-abdominal ultrasound, and CRP levels. According to the 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 ⁽¹¹⁾ included 51 children aged 3-17 years. Their PAS Score was ≥ 6 . They excluded patients with symptoms ≥ 5 days, pregnant patients, immunodeficient patients, and patients with diffuse peritonitis, or an abscess > 5 cm or perforation.

Steiner et al ⁽¹²⁾ 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.

Children with PAS scores ≥ 4 were the main zone of our study and confirmed the diagnosis with the US. All operated cases were scored more than 7 while, while patients who had a score of 4-6 were in 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 scores 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 ⁽¹³⁾ 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.

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 7.5 mg/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 ⁽¹¹⁾, Steiner et al ⁽¹²⁾ depended on IV ceftriaxone and metronidazole or ciprofloxacin and metronidazole during

conservative management. They followed their patients at home on oral amoxicillin/ clavulanic acid or ciprofloxacin and metronidazole or cefdinir and metronidazole for 10 days.

Minneci et al ⁽¹⁵⁾ 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 complete 10 days. Svensson et al ⁽¹⁴⁾ used IV meropenem and metronidazole regimen in hospital 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 of treatment.

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

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

In our study oral intake was restricted only to patients who had severe GIT symptoms such as vomiting, abdominal colic, 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 ⁽¹⁴⁾ and Steiner et al ⁽¹⁵⁾ studies oral intake was restricted for at least 48h. Once the patient tolerated shifting to oral intake and oral antibiotics. Svensson et al ⁽¹¹⁾, Minneci et al ⁽¹²⁾ restricted oral intake during the first 24h of the management. They discharged patients when they became afebrile for at least 24h, were abdominal pain-free, and tolerated oral intake.

During NOM, we stressed frequent examination and meticulous observation of patients, and daily LC & CRP were performed; all to detect any deterioration or complication early. NOM was practiced for a maximum of 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 that 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.

Knaapen M et al, ⁽¹⁶⁾ reported that the median duration of hospital stay was 2.5 days under observation with daily monitoring of patients. Appendectomy was decided once there was a deterioration of symptoms and signs.

While in Armstrong J et al ⁽¹⁵⁾ study the mean duration of hospital stay in patients who had success NOM was 1.5 days while in operated patients was

1.3 days., and In Minneci et al ⁽¹⁷⁾ study the mean duration of hospital stay was 37 h in the NOM group also it was 20 h in an operated group.

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 the inclusion of adult patients only. ⁽¹⁸⁾

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

According to the 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 ⁽¹⁹⁾ revealed that the overall costs were 1-6 times higher in the children subjected to appendectomy when compared with children who had successful NOM.

Conclusion:

Using conservative management of AUA among children aged 4-16 years, proved to be safe, effective, and has 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 parent counseling, the parents can accept the NOM and have their fear alleviated. However, a controlled randomized trial on a bigger number of cases is needed to validate these results.

UNDER PEER REVIEW

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