

Research Article

Use of Antibiotics Alone for Treatment of Uncomplicated Acute Appendicitis in Adults

Ashraf A. Mubarak, Ayman M. Hassanin and Mohamed R. Abd-Ella

Department of Surgery, Minia University, Egypt.

Abstract

Aim: To assess the efficacy of non-operative treatment of uncomplicated acute appendicitis over a period of one year follow-up to increase the amount of evidence supporting the use of antibiotics instead of surgery for treating these patients. **Patients and Methods:** A total of 242 patients were randomly selected out of patients with uncomplicated AA seen in the Department of Surgery at Minia University Hospital between June 2013 and June 2014. All cases were confirmed as uncomplicated AA; using a combination of CT and US. Patients were excluded if they were <12 years old, pregnant, had psychiatric disorders or history of drug abuse. Antibiotic treatment regime included: 1 g ceftriaxone twice daily and 500 mg metronidazole three times daily for the first 48 hours, followed by 500 mg oral ampicillin/sulbactam twice daily and 500 mg metronidazole three times daily for 10 days. Appendectomy was performed if symptoms did not improve within 48 h. Predictors of recurrence were studied including: age, sex, WBC, and presence of appendicolith. **Results:** The median follow-up period for patients was 13 months (range, 11-16 months). Twenty three (9.5%) patients were diagnosed with recurrent appendicitis. Nineteen patients (7.9%) were selected to continue with non-operative treatment. Statistical significance was observed only between presence of appendicolith and recurrence ($p=0.001$). **Conclusion:** Antibiotic treatment can be offered as first-line therapy not only for complicated acute appendicitis but also for uncomplicated acute appendicitis without medical drawbacks other than the unknown risk for long-term recurrence. Therefore, we recommend more patients to be considered for antibiotic therapy instead of surgery.

Keywords: Appendicitis, appendicolith, non-operative, antibiotic treatment, recurrence

Introduction

The most common cause of acute abdomen is acute appendicitis (AA).^[1] For more than a century, appendectomy has been the predominant treatment of AA introduced by McBurney in the 1880's and performed by Grooves in 1883. After that, the procedure has been standardized among surgeons.^[2] Recently, there is increasing interest regarding antibiotic therapy of AA with the development of imaging diagnosis, including computerized tomography and ultrasound. Also, as with all operations, postoperative complications of appendectomy exist, including wound infections, intra-abdominal abscesses, ileus and adhesions. In addition, the mainstay of treatment for other intra-abdominal inflammatory processes, such as diverticulitis, consists initially of conservative management with antibiotics.^[3] Furthermore, new

opportunities for nonsurgical treatment of appendicitis were added by investigations into novel and efficient antibiotics.^[4] So, antibiotic therapy is becoming increasingly important in the treatment of AA.^[5,6] The aim of the present study was to assess the efficacy of non-operative treatment of uncomplicated AA over a period of one year follow-up to increase the amount of evidence supporting the use of antibiotics instead of surgery for treating these patients.

Patients and methods

A total of 242 patients were randomly selected out of patients with uncomplicated AA seen in the Department of Surgery at Minia University Hospital between June 2013 and June 2014. All cases were confirmed as uncomplicated AA; using a combination of CT and US. After diag-

nosis, advantages and disadvantages of appendectomy versus antibiotic treatment were explained to all patients according to their age category and medical status. All patients gave informed consent and the study protocol was approved by Minia Medical College Ethical Committee. Patients were excluded if they were <12 years old, pregnant, had psychiatric disorders or history of drug abuse.

Antibiotic treatment regime included: 1 g ceftriaxone twice daily and 500 mg metronidazole three times daily for the first 48 hours, followed by 500 mg oral ampicillin/sulbactam twice daily and 500 mg metronidazole three times daily for 10 days.^[4] Appendectomy was performed if symptoms did not improve within 48 h. Colonoscopy was performed after 2 months for patients with increased risk of colorectal malignancy (e.g. age \geq 40 years). Predictors of recurrence were studied including: age, sex, WBC, and presence of appendicolith. Patients were divided according to age into 2 groups; <30 years or \geq 30 years and according to WBC count at admission into 2 groups; <12,000 cells/ μ L or \geq 12,000 cells/ μ L.

Study definitions

Failed antibiotic response is defined as “lack of improvement or even worsening within 48 h after initial treatment”.^[4]

Efficacy with antibiotic treatment was defined as “definite improvement without the need for surgery within a median follow-up of 1 year”.^[4]

Statistical analysis

Statistical analyses were performed using SPSS software version 16.0 (SPSS Inc.; Chicago, Illinois, USA). A *p* value of \leq 0.05 was considered statistically significant.

Results

Total number of patients was 242 who accepted to be included in this study; 82 females and 160 males (33.9% and 66.1%,

respectively). Median age was 30 years (range, 12–74 years). Appendicolith was diagnosed in 31 patients (12.8%). Median WBC count at admission was 12,500 cells/ μ L (range, 11,100–14,600). Four patients (1.6%) did not achieve improvement within 48 hours (3 males and one female).

Surgical intervention revealed gangrenous appendicitis in 2 males (0.8%) and catarrhal inflammation in one male and one female (0.8%). There were no intra-abdominal abscesses or other major complications associated with delayed appendectomy. None of them developed postoperative complications. Mean hospital stay was 2.5 ± 1.1 days. Thirty nine patients (16.1%) underwent colonoscopic examination 2 months after successful medical treatment to exclude colorectal malignancy but no malignancies detected. The median follow up period for patients was 12 months (range, 11–10 months).

Thirty of 238 patients (12.6%) experienced pain symptoms during follow up period. Twenty three (9.7%) of these were readmitted to hospital and diagnosed with recurrent appendicitis. For remaining 7 patients (2.9%), their pain was attributed to gynecological and urinary causes. Recurrence observed within 2–6 months of follow up period. In all cases, diagnosis of recurrence and assessment of appendicolith formation were confirmed by CT. No appendicolith was detected in 3 recurrent cases (1.3%) despite its presence at first presentation. Nineteen patients (7.9%) were selected to continue with non-operative treatment and take another course of intravenous antibiotics. The results were favorable with no further symptoms of recurrence. The remaining four patients (1.7%) underwent appendectomy. Surgical intervention revealed catarrhal inflammation in all of them. None of them developed postoperative complications. Mean hospital stay was 2.2 ± 1.2 days. Patient characteristics are shown in table 1.

Table (1): Patients' characteristics.

Characteristics	Recurrent	Non recurrent	p Value
Age:			
<30	10	96	0.06
≥30	8	119	
Sex:			
Male	16	141	0.702
Female	7	74	
WBC: (cell/μL)			
<12,000	11	134	0.176
≥12,000	12	81	
Presence of appendicolith:			
Yes	10	32	0.001
No	13	183	

Discussion

Recently, antibiotic therapy of AA has been proposed by number of authors.^[7,9-11] Some authors recommend interval appendectomy to guard against recurrent appendicitis and possibility of missed malignancy; however, this appeared to be a growing trend in the direction towards the use of antibiotics and avoidance of surgery.^[12,13] Then, the patient may undergo radiologic or endoscopic examination later on to exclude missed malignancy.

The results of this study confirmed that efficacy of antibiotic therapy is not 100%; however, impact on the patient is minimal in failed cases.

Reported failure rates include 27.3% by Salminen et al.,^[14] 23% by Hansson et al.,^[15] 17.7% by Paudel et al.,^[16] 9.2% by Wojciechowicz et al.,^[17] 6.9±4.4% by Liu and Fogg^[18] and 1.2% by Kirkil et al.,^[4] Failure rate in current study was 1.6%. However, failed antibiotic response alone is not sufficient to exclude non-operative therapy as antibiotics are common element of both non-operative and operative management plans.

As regard progression to complicated appendicitis and risk of surgical site infection, Varadhan et al.,^[19] demonstrated decreased risk of both perforation and

surgical complications with antibiotic treatment. In another study by Salminen et al.,^[14] 70% of 207 patients with failed antibiotic treatment who subsequently underwent appendectomy, only 5 had complicated AA. Also, Kirkil et al.,^[4] did not report any surgical site infection in patients underwent appendectomy after failed non-operative treatment. On the other hand, Teixeira et al.,^[19] noted increased risk of surgical site infection with appendectomy delay. In our study, surgical site infection was not found in patients who failed to respond to non-operative treatment and underwent appendectomy. This may be explained by initial antibiotic delivery for at least 4 h prior to appendectomy and antibiotic efficacy which minimize the risk of progression to complicated AA.

Regarding recurrence rates, 20% recurrence rate reported by Varadhan et al.,^[19] 14.2%±10.6% by Liu and Fogg,^[18] 10.2% by Kirkil et al.,^[4] and 0% by Kaminski et al.,^[20] However, Salminen et al.,^[14] reported no recurrence during one year follow up period. In the present study, recurrence rate was 9.9% during median follow-up period of 12 months. Length of follow up period may explain different recurrence rates between different studies. In addition, nineteen recurrences (9.9%) in the current study were treated with another course of antibiotics. So, the current study agreed

with data from previous studies and also confirmed that non-operative treatment for uncomplicated AA does not increase the risk of recurrence or adversely affect the patient's prognosis.

Factors associated with increased risk of recurrence with complicated AA include retained fecal stones (appendicolith), elevated C-reactive protein levels, high differential count of banded neutrophils and partial small bowel obstruction on admission.^[11-13]

However, the most important factor for increased risk of recurrence with uncomplicated AA is the presence of an appendicolith.^[4] Appendicolith as predictive factor for recurrence was studied by Lien et al., along with age, gender, comorbidities, presenting symptoms, laboratory data, appendicitis type and duration of antibiotic treatment but reported that male gender is the only significant factor associated with recurrence with no significant association between appendicolith and recurrence.^[14] On the other hand, significant association between calcified appendicolith and recurrence was reported by Tsai et al.,^[15] who investigated the CT findings between patients with and without recurrent appendicitis in a retrospective study, and by Kırkıl et al.,^[4] who reported association between appendicolith and recurrence. The current study observed significant negative association between presence of appendicolith and recurrence ($p=0.001$). Moreover, no appendicolith was detected in 3 recurrent cases (1.3%) despite its presence at first presentation by CT. These different results means that the relationship between appendicolith and recurrence is not yet documented.

Tumors are one of the causes of AA. However, malignancy risk is very low in appendectomy specimens; consequently this relationship cannot counteract the promotion of antibiotic treatment for uncomplicated AA.^[4] Two of 369 AA patients with malignancies of appendix or colon were discovered by Hansson et al.,^[4] only at the time of appendectomy. So, risk of malignancy cannot be considered an argument against antibiotic treatment for

cases of uncomplicated AA. In this study, colonoscopy was performed according to colorectal cancer screening recommendations and no appendiceal or colorectal malignancy was detected.

Our results indicate that antibiotic therapy for uncomplicated AA is an effective and successful in nearly 90% of all patients according to the results of the present and previous studies. Although recurrence is unpleasant complication following antibiotic treatment of uncomplicated AA, it often presents within short period of follow up, can be treated efficiently with administration of second course of antibiotics and does not affect the patient's prognosis. Lastly, presence of appendicolith should not be an argument against non-operative treatment for patients with uncomplicated AA. In conclusion, antibiotic treatment can be offered as first-line therapy not only for complicated AA but also for uncomplicated AA without medical drawbacks other than the unknown risk for long-term recurrence. Therefore, we recommend more patients to be considered for antibiotic therapy instead of surgery.

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