

## Comparison between Antibiotic Treatment to Surgical Treatment in Uncomplicated Appendicitis: An Egyptian Experience

Shady ElGhazaly Harb, Sherif Mohamed Mokhtar

Department of General Surgery, Emergency Unit  
Faculty of Medicine (Kasr AlAini), Cairo University

### ABSTRACT

**Introduction:** Since the early 20th century, treatment of acute appendicitis has been primarily surgical as appendectomy. Several studies suggest appendectomy may not be necessary for patients with acute uncomplicated appendicitis, with treatment using antibiotics being sufficient. **Patients and method:** This is a Prospective randomized clinical trial done on adult patients presented to Kasr El-Aini Hospital emergency department with clinically suspected, uncomplicated appendicitis, to compare antibiotic treatment to surgical treatment in uncomplicated appendicitis, from May 2016 to August 2016. **Results:** A total of 150 patients satisfied our criteria and were included in the study. Of the 67 patients in the antibiotic group, 62 (92.5%) did not require appendectomy within the follow up period of 3 months. Despite having recurrent appendicitis and delayed operations, only 2 patients of the 5 who eventually underwent appendectomy had postoperative surgical complications in the form of superficial surgical site infection. While in the surgical group, 32 patients (39%) had various postoperative complications ranging from surgical site infection to intra-abdominal abscess. No patient in the antibiotic group developed an intra-abdominal abscess, including those who underwent delayed appendectomy. **Conclusion:** Antibiotic therapy is an effective form of treatment that can be offered to uncomplicated appendicitis patients in hospitals in Egypt. It has a high success rate, and a low rate of complications in case they required surgery later in the course of the disease. Further studies in the form of randomised controlled trial should be attempted with larger numbers of patients and longer periods of follow up.

**Key Words:** Uncomplicated appendicitis, conservative treatment, surgical treatment

### INTRODUCTION

Acute appendicitis (AA) is the most common cause of emergency surgery, with a lifetime prevalence of 7%–8% with highest incidence and the second decade of life<sup>(1)</sup>. Since the early 20th century, treatment of acute appendicitis has been primarily surgical as appendectomy. The surgical management of AA has greatly reduced the mortality associated with the disease; however the risk of complications is inherent to surgical treatment. Most commonly, these complications include wound infection, intra-abdominal abscess formation, and prolonged ileus<sup>(2)</sup>.

Overall complication rates in adults are 11.1% with open appendectomy and 8.7% laparoscopically<sup>(3)</sup>, although considered a safe operation it still has a mortality ranging from 0.07 to 0.7% in uncomplicated cases, and up to 2.4% in perforated appendicitis<sup>(4)</sup>.

The operative management of appendicitis varies with the extent of disease at presentation. The three general categories of disease are those

with appendicitis with no evidence of perforation, those with perforated appendicitis, and those who present with a well defined abscess<sup>(5)</sup>.

The decrease in mortality achieved by a single prevented perforation may be therefore attenuated by an high incidence of negative appendectomy, especially in elderly and frail patients<sup>(6,7)</sup>. In fact, Andersson recently showed from a population-based case-control study that appendicitis is only responsible for a small proportion of the deaths after appendectomy. Comorbidity and negative appendectomy were strongly associated with mortality, suggesting that comorbidity, diagnostic failure, and anesthesia surgical trauma may play an important role<sup>(8)</sup>.

Other authors suggest that appendectomy may not be necessary for the majority of patients with acute uncomplicated appendicitis, as the condition resolves spontaneously in many patients and may be treatable with antibiotics alone in other patients<sup>(9)</sup>. This approach has many advantages, including high success and low recurrence rates, reduced morbidity and mortality, less pain,

shorter hospitalization and sick leave, and reduced costs<sup>(10)</sup>.

Several randomized controlled trials, cochrane reviews and meta-analysis have been published confirming the feasibility of this new strategy. Mortality was reported to be as low as 0.2%, with recurrence occurring in just 14.4% of cases. However, the role of antibiotic therapy has been established in uncomplicated appendicitis, with surgery still forming the mainstay of treatment in complicated cases<sup>(11,12)</sup>.

No study to date has been done to evaluate the feasibility of conservative treatment for appendicitis in the Egyptian population. This study, therefore, aims to compare antibiotic treatment to surgical treatment in uncomplicated appendicitis, amongst patients presenting to Kasr ElAini Medical School Hospital, Cairo

## PATIENTS AND METHOD

This is a Prospective randomized clinical trial done on adult patients presented to Kasr El-Aini Hospital emergency department with clinically suspected, uncomplicated appendicitis, as confirmed by abdominal ultrasound from May 2016 to August 2016. An informed consent was obtained from the patients who fit the criteria and were assigned into either surgical or antibiotics group according to their own choice the patients choice considered as randomization, the randomization is performed in 1:1 equal allocation ratio.

All adult patients admitted to the emergency department with a clinical suspicion of uncomplicated appendicitis will be studied carefully by attending surgeons at the emergency departments the study includes clinical history, physical investigation and laboratory blood tests (blood hemoglobin, leukocyte count, and plasma C-reactive protein and liver and kidney functions) as well as urine analysis are undertaken before any pain medications are administered at emergency ward. If clinical history and physical examination and ultrasound examination suggest that the patient has uncomplicated appendicitis, the patient is eligible for inclusion in the study and after signed informed consent is obtained the patients are informed of the protocol and invited to participate. Exclusion criteria includes Age < 18 years or > 60 years, Pregnancy or lactating Inability to co-operate and give informed consent

Serious systemic illnesses well as those diagnosed as complicated appendicitis by abdominal ultrasound. Abdominal ultrasound was performed to exclude complicated appendicitis in the form of perforation, which is indicated by pelvic fluid collection, or inflammation in abdominal cavity lining, or the beginning of mass forming around the appendix.

After confirming the diagnosis of uncomplicated AA the patients will be subjected to either one of the interventions below

### Interventions

#### Surgical treatment

After randomization to undergo operative treatment, open appendectomy will be performed by standard technique using a McBurney right lower quadrant muscle splitting incision. Prophylactic antibiotic as a single dose of 1.5 g cefuroxime and 500 mg metronidazole is administered approximately 30 min preoperatively. The histopathological examination of the appendix will be performed and the histological diagnosis of acute appendicitis requires involvement of the muscularis of the appendix (transmural neutrophil invasion).

#### Antibiotics group

Patients in this group received intravenous ceftriaxone 1g twice daily, as well as intravenous 500mg metronidazole twice daily, for 3 days. The patients were followed up closely and their vital signs recorded in a special follow up card, as well as serial total leukocytic counts (TLC). Ultrasound was repeated on day 3 to ensure the condition is improving. After day 3, and if the patients were clinically improving, they were converted to oral antibiotics in the form of levofloxacin 500mg twice daily and metronidazole 500mg 3 times daily.

#### The primary end-point

Success of the randomized treatment in this trial is defined in the antibiotic treatment arm as the resolution of acute appendicitis with antibiotic treatment resulting in discharge from the hospital without the need for surgical intervention and no recurrent appendicitis during a minimum follow-up of three months.

The primary endpoint of treatment success in this trial is defined in the operative treatment arm as defined as successful appendectomy evaluated to be 100%.

### Follow up

Patients were assessed clinically at day 3 before their discharge, if they were fit for discharge or needed to stay under observation. They were instructed to come back if they felt unwell at any given moment. They were also followed up in the emergency department outpatient clinic every week for 3 months after their discharge. Recurrent acute appendicitis was diagnosed on a clinical basis. Patients treated with antibiotics who had a suspected recurrence of appendicitis always underwent appendectomy. The diagnosis of recurrent appendicitis was confirmed by surgical and histopathological examination of the resected specimen.

### Statistical Analysis

For computational reasons, the success rate for surgery was assumed to be 99%. Prior similar studies found success rates for antibiotic treatment of approximately 70% to 80%.<sup>7,8</sup> Thus, we anticipated a 75% success rate in the antibiotic therapy group and a 24% (95% CI, 75%-99%). Categorical variables were characterized using frequencies and percentages, continuous variables as means and standard deviations or, if the data were skewed, as medians with 25th and 75th percentiles. Statistical significance for categorical data was tested using the Pearson  $\chi^2$  test. Differences between groups for normally distributed variables (hemoglobin level, leukocyte count, and creatinine level) were tested using the independent sample t test. The Mann-Whitney test was used for variables not normally distributed. Data were analyzed using IBM® SPSS® Statistics version 22 (IBM® Corp., Armonk, NY, USA).

## RESULTS

A total of 150 patients satisfied our criteria and were included in the study. Eighty three patients chose to receive appendectomy and 67 patients chose to join the antibiotic therapy group. Of the 83 patients in the surgical group, 10 cases (12%) did not have histopathological evidence of acute appendicitis in the resected specimens. Six patients (7%) underwent a laparoscopic appendectomy.

Four patients in the surgical group were found to have complicated appendicitis during their surgery in the form of perforation. Fifteen patients were lost to follow-up in the surgical group.

These 15 patients in the surgical group were included in the primary end point analysis because they had undergone appendectomy.

Of the 67 patients in the antibiotic group, 62 (92.5%) did not require appendectomy within the follow up period of 3 months. Five patients (7.5%) in the antibiotic group underwent surgical intervention 3 months within their initial presentation, 3 of them were due to deterioration of their clinical condition within the first 3 days. One of those patients was found intraoperatively to have perforated appendix at the apex, while the other 2 had gangrenous base. The other 2 had appendectomy later on after their discharge due to recurrent attacks of pain, and postoperative pathology revealed recurrent appendicitis. Only 7 patients of the antibiotic group were lost to follow up.

Despite having recurrent appendicitis and delayed operations, only 2 patients of the 5 who eventually underwent appendectomy had postoperative surgical complications in the form of superficial surgical site infection. While in the surgical group, 32 patients (39%) had various postoperative complications ranging from surgical site infection to intra-abdominal abscess. No patient in the antibiotic group developed an intra-abdominal abscess, including those who underwent delayed appendectomy.

The 30-day mortality rate in the surgical group was 1 patient (1.2%) who died at day 5 in the ICU due to pulmonary embolism. No deaths occurred in the antibiotic group within the follow up period.

There were 26 surgical site infections (3 intra-abdominal, 5 deep incisional, and 18 superficial). Four of those patients had delayed healing of the incision and 3 of them complained of persistent incisional pain noted at the 2-month follow-up. Of the other 6 patients who had postoperative complications in the surgical group; 2 suffered from DVT and consequent pulmonary embolism (one of which died on day 5), and 4 had atelectasis and chest infection which led to a longer hospital stay. Those patients had a noticeably higher BMI than the rest of the patients (mean BMI 38).

The duration of hospital stay was shorter in the surgical group (median 2 days) than in the antibiotic-treated group (median, 3 days).

## DISCUSSION

Acute appendicitis is one of the most common urgent conditions seen in general surgery practice. Although the exact mechanisms leading to this condition are still obscure, it is likely that luminal obstruction by external (lymphoid hyperplasia) or internal (appendicolith) compression plays a key pathogenetic role<sup>(13)</sup>.

Despite small sample size and short follow up period, the preliminary results of antibiotic therapy of appendicitis in Egypt seem promising. This is indicated by the high success rate of antibiotic therapy recorded by this study (92.5%), with none of those who needed surgical intervention in this group having major complications postoperatively. Therefore, patients in Egyptian hospitals, with clinically and radiologically proven uncomplicated appendicitis, should be offered treatment either by antibiotic therapy alone or appendectomy. Consequently, blood and lymph flow is diminished, and necrosis and perforation follow. As these events occur over time, it is conceivable that early surgical intervention prevents progression of disease. However, epidemiologic studies on incidence of nonperforated and perforated Acute appendicitis suggest that nonperforated and perforated Acute appendicitis may have different pathogenetic mechanisms strongly supporting our study hypothesis in re-evaluating the dictum that surgical removal of the appendix is always necessary for acute appendicitis<sup>(14)</sup>. The hypothesis that the majority of patients with uncomplicated acute appendicitis can be cured with wide-spectrum antibiotics avoiding a large number of unnecessary appendectomies had been supported by previous randomized studies<sup>(15)</sup>.

Although this topic has been reported by a large number of studies in recent years, to our knowledge, this is the first study to address efficacy of conservative antibiotic treatment of appendicitis as compared to the standard surgical approach in Egypt.

This preliminary prospective study of cases of appendicitis presenting to Kasr ElAini Hospital emergency department had a smaller number of cases as compared to other international studies. Nevertheless, it can form a basis for further investigation with larger sample size, and a longer period of follow up in order to fully evaluate the

efficacy of conservative antibiotic treatment with the limited resources we are faced with in Egypt.

The failure rate of conservative antibiotic therapy was just 7.5% (5 patients out of 67 had to undergo surgery) in the first 3 months follow up period. Although this seems significantly lower than the accepted failure rate of 24% at one year follow up, the small sample size and limited follow up period of 3 months make it difficult to confirm this low failure rate in favour of antibiotic therapy. Recurrent attacks are expected within 1 year of follow up in most previous studies. Nevertheless, this can be considered an indicator for the feasibility and efficacy of conservative treatment in Egyptian hospitals. Moreover, 2 of the 5 cases which required appendectomy in the antibiotics group did not have complicated appendicitis at the time of the procedure. This indicates that further trial of antibiotic therapy might have spared us the need for operation.

Meanwhile, the relatively high postoperative complication rate in the surgical group (39%) reflects the relatively high risk the patients face in this setting, which can be attributed to multiple factors. This in turn supports the necessity to examine alternative lines of treatment, such as conservative, to reduce possible morbidity and extra costs.

## CONCLUSION

Antibiotic therapy is an effective form of treatment that can be offered to uncomplicated appendicitis patients in hospitals in Egypt. It has a high success rate, and a low rate of complications in case they required surgery later in the course of the disease. Further studies in the form of randomised controlled trial should be attempted with larger numbers of patients and longer periods of follow up.

## REFERENCES

1. Addis DG, Shaffer N, Fowler BS, et al. The epidemiology of appendicitis and appendectomy in the United States. *Am J Epidemiol* 1990; 132:910–25.
2. Al-Omran M, Mamdani M, McLeod RS. Epidemiologic features of acute appendicitis in Ontario, Canada. *Can J Surg* 2003;46:263–8

3. Guller U, Hervey S, Purves H, et al. Laparoscopic versus open appendectomy: outcomes comparison based on a large administrative database. *Ann Surg* 2004; 239:43–52.
  4. Svensson JF, Hall NJ, Eaton S, et al. A review of conservative treatment of acute appendicitis. *Eur J Pediatr Surg* 2012;22:185–94.
  5. Peter SDS, Snyder CL. Seminars in Pediatric Surgery Operative management of appendicitis. *Semin Pediatr Surg* . 2016;25(4):208–11.
  6. Blomqvist P, Andersson R, Granath F, et al. Mortality after appendectomy in Sweden, 1987–1996. *Ann Surg*. 2001;233:455–460.
  7. Flum D, Koepsell T. The clinical and economic correlates of misdiagnosed appendicitis: nationwide analysis. *Arch Surg*. 2002;137:799–804.
  8. Andersson MN, Andersson RE. Causes of short-term mortality after appendectomy: a population-based case-controlled study. *Ann Surg*. 2011;254:103–107.
  9. Mason RJ, Moazzez A, Sohn H, et al. Meta-Analysis of randomized trials comparing antibiotic therapy with appendectomy for acute uncomplicated (no abscess or phlegmon) appendicitis. *Surg Infect*. 2012;13:74–84.
  10. Sakorafas G, Mastoraki A, Lappas C, et al. Conservative treatment of acute appendicitis: heresy or an effective and acceptable alternative to surgery? *Eur J Gastroenterol Hepatol*. 2011;23:121–127.
  11. Aarabi S, Sidhwa F, Riehle KJ, Chen Q, Mooney DP. Pediatric appendicitis in New England: epidemiology and outcomes. *J Pediatr Surg* 2011;46:1106e14.
  12. Kirby A, Hobson RP, Burke D, Cleveland V, Ford G, West RM. Appendectomy for suspected uncomplicated appendicitis is associated with fewer complications than conservative antibiotic management: a meta-analysis of post-intervention complications. *Journal of Infection*. 2015 Feb 28;70(2):105–10.
  13. Farahnak M, Talaei-Khoei M, Gorouhi F, Jalali A: The Alvarado score and antibiotics therapy as a corporate protocol versus conventional clinical management: randomized controlled pilot study of approach to acute appendicitis. *Am J Emerg Med* 2007, 25(7):850–852.
  14. Shrestha B: Antibiotics versus surgery for appendicitis. *Lancet* 2011, 378(9796):1067. author reply 1068.
  15. Vons C, Barry C, Maitre S, Pautrat K, Leconte M, Costaglioli B, Karoui M, Alves A, Dousset B, Valleur P, Falissard B, Franco D: Amoxicillin plus clavulanic acid versus appendectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial. *Lancet* 2011, 377(9777):1573–1579.
-