

Prospective Study on the Efficacy and Safety of Antibiotics for Treating Patients with Acute Appendicitis (NOTA) Non Operative Treatment of Acute Appendicitis

LUQMAN ALI BAJWA¹, MUHAMMAD ASJAD², MUHAMMAD IMRAN MANZOOR³, NOOR-UL-MUBEEN⁴, .HASSAN SHAUKAT⁵, ZEESHAN AHMAD⁶

^{1,2,4,5}SR Surgery, Services Hospital, Lahore

³Assistant Professor Surgery, Services Institute of Medical Sciences, Lahore

⁶Assistant Professor Surgery Lahore Medical & Dental College/GTTH, Lahore

Correspondence to Dr. Luqman Ali Bajwa, SR Email: dr.luqman@yahoo.1com Cell: 0332-8373997

ABSTRACT

Background: In surgical practices, the commonest acute condition is seen to be the acute appendicitis. The appendectomy being the well-known surgical treatment of appendicitis is also linked to all complications of surgery.

Aim: To assess efficacy and safety of antibiotic treatment in patients with acute appendicitis.

Methods: This observational prospective cohort study was conducted on 150 patients with right lower abdominal pain and diagnosed cases of acute appendicitis. All the patients >15years of age with acute appendicitis after full filling inclusion/exclusion criteria were included.

Results: A total of 150 patients were recruited for this study. There were a total of 105(70%) females and 45(30%) were male. The NOTA failure rate was observed in short term (<7days) and reported in 18(12%) patients, out of these patients 12(66.7%) failed NOTA with antibiotics as having probable appendicitis at admission, and 6(33.3%) had equivocal acute appendicitis. No reoccurrence was reported within 15 days in cases with initial failure and then operated within seven days. Of these patients almost 15(10%) recurrence episodes were recorded in 6 months follow-up. Ten were treated successfully with the further antibiotics cycles. Only 4 further recurrences were observed at one-year time.

Conclusion: The appropriate addressing of the treatment to the cases of acute appendicitis from the initial evaluation and diagnosis; antibiotic treatment will be safer and effective.

Keywords: Acute appendicitis (AA), perforation, complication incidence, appendectomy, antibiotics

INTRODUCTION

In surgical practices, the commonest acute condition seen is the acute appendicitis. In classic literature, the surgical appendectomy is considered to be the main treatment for the appendicitis, even if the case is not authenticated with the diagnoses. Conversely, on histopathology, the appendix is observed to be disease free in 15 to 30% of the entire cases^{1,2}. After appendectomy certain surgical complications i.e., wound infection, pneumonia, intestinal obstruction and the tubal infertility in females are linked to the appendectomy method that's why, the conservative treatment may be useful or beneficial. The safety implications were reported with non-operative management of the suspected acute appendicitis. On the other hand, the perforated appendicitis and intra-abdominal abscesses are the risks increased with delaying the surgery, certain risks increase after the surgery including intra-abdominal abscesses, adhesive small bowel obstruction and infertility etc. The surgical and conservative treatments are comparable and their utilization attracts a considerable debate in fewer acute appendicitis cases^{3,4,5}.

If NOTA is opted, it requires accurate diagnosis and appropriate patients assessment to be selected for the treatment. The spontaneous resolution of appendicitis with antibiotics has a classical history as of Alfred et al in 1908 mentioned that the most of the appendicitis cases recovers greatly once treated in tentative medical manner^{6,7,8}.

The morbidity and mortality associated with negative appendectomy should be weighed against the risk of perforation due to delayed treatment. The appendectomy itself carries risk due to all the complications of surgery linked to it^{9,10}.

The main aim of study was to assess efficacy and safety of antibiotic treatment in patients with acute appendicitis.

MATERIAL AND METHODS

This observational prospective cohort study was conducted on 150 patients with acute appendicitis. They were further requested to take non-operative oral antibiotic therapy with Ciprofloxacin + Flagyl. The exclusion criteria includes all patients with ALVARDO 9-10, diffuse peritonitis, on antibiotic documenting allergy, previously recommended ongoing antibiotic therapy, history of appendectomy and pregnancy. The study was conducted during 2017-2018 in Services Hospital, Lahore. All the demographic and diagnostic findings were noted from the entire sampled individuals. Certain tests performed including the complete blood count with differential, abdominal ultrasound and abdominal CT scan. The standard operating procedures were opted while practicing all operative and diagnostic or clinical tests. All the susceptible acute appendicitis patients having ALVARDO 5-8 with no need of immediate surgery were put on non-operative antibiotic treatment. (NOTA). To measure the susceptible acute appendicitis an Alvarado scoring scheme¹¹ was opted to categorize the patients. If

the score ranges between 5-6, than it is equivocal for acute appendicitis, a score of 7-8 will indicate the probable appendicitis and a score of 9-10 will indicate highly probable appendicitis(excluded from study). The patients were put on follow-up for regular visits and their findings on each of the visit were recorded. The ethical approval was taken from hospital ethical committee.

Statistical analysis: All the information collected or noted from all the participants were then entered electronically to MS EXCELL sheets and stored in computer. Latterly, this data was exported in SPSS format to be analyzed by using SPSS version 21.0. Descriptive statistics were applied by calculating mean and standard deviation. Frequency distribution and percentages were performed for all qualitative variables.

RESULTS

A total of 150 patients were recruited for this study. In this study there was a total of 105(70%) females and 45(30%) were males. The detailed summary of demographic and diagnostic findings is given in table 1.

About 73(48.6%) of the patients were having the Alvarado score ranging 5-6, 77(51.4%) were having score of 7-8. The entire patients underwent non operative treatment (NOTA). The NOTA failure rate was observed in short term (<7days) and reported 18(12%) out of these patients 12(66.7%) failed NOTA with ciprofloxacin+

metronidazole were identified as having probable appendicitis at admission, and 6(33.3%) as equivocal for acute appendicitis. No reoccurrence was reported at 15 days findings in cases with initial failure and then operated within seven days. Of these patients almost 15 (10%) recurrence episodes were recorded on 6 months follow up. Ten were treated successfully with the further antibiotics cycles and 5 were operated. Only 4 further recurrences were observed at one-year time. More on the outcome results of a year follow up with the failure (in seven days) and relapse rate is given in table 2.

Table 1: Summary of demographic and diagnostic characteristics

Characteristics	n (%)
Age	32.14±7.59
Gender (M / F)	105 (70%) / 45 (30%)
Female to male Ratio	3:1
Ultra Sound (positive) *	108 (72%)

*US positive for at least one of the following: enlarged appendix >6 mm, fluid-filled appendix, loculated pericecal fluid, free intraperitoneal fluid, appendicolith, increased periappendiceal echogenicity, hypoechoic appendix, echogenic submucosa, lack of compressibility, inflamed periappendiceal fat.

Table 2: Results: follow up with the failure (in seven days) and relapse rate

Time	7 Days	15 days	6 Months	1 year
Rate	12%	0%	10%	2.6%
frequency	18/150 failure	0/150 recurrence	15/150 recurrence	4/150 recurrence
Therapy	18 OR <7d†	—	5/15 OR 10/15 NOM	4 OR

* † patients with initial failures underwent surgery within 7 days. **OR: operating room. Total failure rate of NOTA was 18% , 27 patients out of 150 underwent surgery in 1 year.

DISCUSSION

The study was conducted to assess the efficacy and safety of antibiotic treatment (ciprofloxacin and metronidazole) in patients with acute appendicitis. We not only reported the efficacy and safety but also the recurrence, relapse and the failure rates of the non-operative treatment options. Various Meta-analysis in literature reported various findings on the NOTA in recent years. One of which was published by Varadhan et al¹² had reported antibiotic therapies or treatment against the surgeries for acute appendicitis. He observed the antibiotic therapy for almost 350 patients of suspected acute appendicitis and reported 68% of the success rate by opting the antibiotic therapy alone. Similarly another meta analysis based on the antibiotic use alone in treating the uncomplicated acute appendicitis, that contains almost 1200 patients with failure rate of 6.9% ± 4.4% when treated with antibiotics alone and the recurrent rate of appendicitis of 14.2% ± 10.6 respectively. Though another systematic review, in 2011, determined that appendectomy remains the standard of treatment of acute appendicitis because the reported rate of success for patients treated with antibiotics alone was 73.4% versus 97.4% for those treated with appendectomy¹³. Another RCTs meta-analysis conducted by the Mason et al¹⁴ reported that the NOTA of uncomplicated appendicitis

with antibiotics was linked with a significantly lesser obstacles, better pain control, and shorter sick leave, but the overall had an inferior efficacy, due to the higher rate of recurrence than appendectomy. We also analyzed and observed the antibiotic therapy efficacy of acute appendicitis while comparing it with the surgery. We conclude that the preliminary results of non surgical approach can be safe and practical, thereby reducing impediments, post-treatment pain, recovery time, and expenses, the low efficacy made palpable by the treatment failure rates and acute appendicitis recurrences meant that antibiotic routines cannot be recommended as a workable alternate to surgery^{15,16}.

Considering the fact that this topic is of worth debate and the implications or practices on daily bases in clinic might create an issue of importance. We have reported in our study with the relapse rate of almost 13.3% at one year has proven better than the chance. The high success rate has proven the score efficacies. In our study it might be of biasedness by using the Alvarado score, given the predominance of females in our study because Alvarado score has been noted to significantly over-predict appendicitis in females¹⁶. Though in our view and practice, the combination of all scores like Alvarado and AIR might reduce the risk

significantly of over-predicting acute appendicitis and grasp a diagnostic enactment as highly reliable as a CT scan, thus evading the routine use of CT and dipping the costs and hospital resources utilization and the radiation/contrast exposure potential risks. Similar to our findings, a study conducted on 941 consecutive patients with suspected acute appendicitis, the AIR score with an area under the receiver operating characteristic curve of 0.96 performed significantly better than the area under the curve of 0.82 of the Alvarado score ($P < 0.05$)^{17,18}.

CONCLUSION

We may conclude from our study that that the appropriate addressing of the treatment to the cases from the initial evaluations, antibiotic treatment will be a safer and effective. To a certain time of follow up, the recurrence rates of suspected acute appendicitis NOM treated with antibiotics is lesser and safely effective in treating further on antibiotic regimens.

REFERENCES

1. Deutsch A, Shani N, Reiss R. Are some appendicectomies unnecessary? An analysis of 319 white appendices. *J R Coll Surg Edinb*. 1983;28:35–40.
2. Malik A, Bari S. Conservative management of acute appendicitis. *J Gastroin- test Surg*. 2009;13:996–970.
3. Pieper R, Kager L, Nasman P. Acute appendicitis: a clinical study of 1018 cases of emergency appendectomy. *Acta Chir Scand*. 1982;148:51–62.
4. Eriksson S, Granstrom L. Randomized Controlled Trial of appendectomy ver- sus antibiotic therapy for acute appendicitis. *Br J Surg*. 1995;82:166–169.
5. Styrud J, Erikson 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
6. Stengel A. Appendicitis. In: Osler W, McCrae T, eds. *Modern Medicine, Volume V: Diseases of the Alimentary Tract*. Philadelphia: Lea & Febiger; 1908.
7. Andersson R. The natural history and traditional management of appendicitis revisited: spontaneous resolution and predominance of prehospital perforations imply that a correct diagnosis is more important than an early diagnosis. *World J Surg*. 2007;31:86–92.
8. Barber M, McLaren J, Rainey J. Recurrent appendicitis. *Br J Surg*. 1997;84:110–112.
9. Blomqvist P, Andersson R, Granath F, et al. Mortality after appendectomy in Sweden, 1987–1996. *Ann Surg*. 2001;233:455–460.
10. Flum D, Koepsell T. The clinical and economic correlates of misdiagnosed appendicitis: nationwide analysis. *Arch Surg*. 2002;137:799–804.
11. Coursey CA, Nelson RC, Patel MB, et al. Making the diagnosis of acute appen- dicitis: do more preoperative CT scans mean fewer negative appendectomies? A 10-year study. *Radiology*. 2010;254:460–468.
12. Varadhan KK, Humes DJ, Neal KR, et al. Antibiotic therapy versus appendec- tomy for acute appendicitis: a meta-analysis. *World J Surg*. 2010;34:199–209.
13. Wilms I, de Hoog D, de Visser D, et al. Appendectomy versus antibi- otic treatment for acute appendicitis [review]. *Cochrane Database Syst Rev*. 2011:CD008359.
14. 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.
15. Ansaloni L, Catena F, Coccolini F, et al. Surgery versus conservative antibi- otic treatment in acute appendicitis: a systematic review and meta-analysis of randomized controlled trials. *Dig Surg*. 2011;28:210–221.
16. Ohle R, O'Reilly F, O'Brien KK, et al. The Alvarado score for predicting acute appendicitis: a systematic review. *BMC Med*. 2011;9:139.
17. de Castro SM, U" nlu" C, Steller EP, et al. Evaluation of the appendicitis in- flammatory response score for patients with acute appendicitis. *World J Surg*. 2012;36:1540–1545.
18. Nelson DW, Causey MW, Porta CR, et al. Examining the relevance of the physician's clinical assessment and the reliance on computed tomography in diagnosing acute appendicitis. *Am J Surg*. 2013;205:452–456.