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# RANDOMISED CLINICAL TRIAL OF PRIMARY ANTIBIOTICS VERSUS SURGERY IN CASES OF ACUTE APPENDICITIS

Surgery

**DR.ABBAS MUSTAFA** M.S (SURG.), FRCS ASSOCIATE PROFESSOR DEPT. OF SURGERY VIMS, PAWAPURI, NALANDA, BIHAR

## ABSTRACT

Recent advancement in diagnostic technology and availability of effective antibiotics provide us an opportunity to revise our approach in the management of acute appendicitis. This clinical trial was done on 200 patients of acute appendicitis, according to set criteria, 20% underwent primary surgery and 80% primary conservative (antibiotics) treatment. 90% of those treated conservatively recovered, 10% needed surgery within 48 hrs. due to treatment failure and 11.25% were operated for recurrence during one year follow up.

Conservative (Antibiotic first) approach is safe in majority of the cases, immediate surgery in all cases of acute appendicitis is not rationale and should be revised.

## KEYWORDS:

Appendicitis, Antibiotics, Appendicectomy,

**Introduction:**

For decades traditionally, the standard treatment of acute appendicitis has been Appendicectomy. Appendicitis is the most common reason for emergency abdominal surgery, with a lifetime incidence of 7 to 14%. However, there is growing interest in non-operative treatment of acute non-perforated appendicitis with antibiotics.

Recent improvements in both the quality and availability of diagnostic imaging allow better preoperative characterization of appendicitis, including the severity of inflammation, size of the appendix, and presence of extra luminal inflammation, phlegmon , or abscess.1-3 These advances permit preoperative stratification of appendicitis severity, which can be used to direct care [4-6] These imaging advances, in conjunction with the availability of broad-spectrum antibiotics, allow for the identification of a subset of patients with uncomplicated appendicitis that can be treated successfully with antibiotics alone. The purpose of this study was to investigate the feasibility of non-operative management of uncomplicated acute appendicitis.

Several recent European randomized controlled trials suggest that therapy with antibiotics alone is a safe treatment option for appendicitis.[7-11] Appendectomy is still recommended for most people with uncomplicated appendicitis, but patients should be informed about options, and an antibiotics-first strategy may be considered in those who have strong preferences for avoiding an operation or who have contraindications to surgery.

**Methods:**

**Study design –**

This is a prospective non-randomized clinical trial comparing conservative management with antibiotic therapy alone in patients with acute appendicitis diagnosed according to the established practice. The attending physicians' decision was based on clinical history and examination, the use of Alvarado scoring, laboratory test and ultrasonography and/ or computed tomography [18,19] Alvarado scores range from 1 to 10 , with score above 4, indicating greater risk of appendicitis. when the scores is less than 4, appendicitis is uncommon and imaging or other intervention were avoided. Patients admitted to our hospital who met the following criteria were eligible for enrollment for non-operative treatment.

1- Age-12 to 70 years
2- Less than 36 hours of abdominal pain
3- White blood cells count less than 16,000 cell/mm
4- Radiographic imaging by ultrasound or CT abdomen with an Appendicular diameter of less than 12mm.
5- Exclusion criteria of the study include a positive pregnancy test, diffuse peritonitis on clinical examination or a history of chronic intermittent abdominal pain.

**INTERVENATIONS TREATMENT PLANS :-**

Those who did not fulfilled above criteria were treated with surgery (laparoscopic/ open appendicectomy. Non operative management consists of hospital admission with minimum of 48hrs of i.v. antibiotics (i.e Ceftriaxone/ Piperacillin - Tazobactum and Metronidazole or Ciprofloxacin with Metronidazole if the patient is allergic to Penicillin) . During this time patient received intravenous fluids with no oral diet.

As the medicines are administered, the patients are judged according to patient's clinical status Improvement. Those who improved after 48hrs were discharged to continue with oral antibiotics (Ciprofloxacin 500mg/Ofloxacin BD and Metronidazol 400mg TID) for a total duration of 10 days. Evidence of clinical worsening like increased severity of pain or systemic signs of sepsis or failure to show any clinical improvement (e.g. decreased tenderness resolution of fever nausea or vomiting ) within 48hrs of iv antibiotics is decided as a failure of non-operative management and patient were switched to surgical therapy either with open or Laparoscopic Appendisectomy . Those patient who returned after discharge with complain of pain in abdomen and re-evaluation of them suggested the diagnosis of Appendicitis they underwent urgent open/ Laparoscopic Appendectomy. Surgical management protocol was hospital admission of patient and initiation of IV Fluids and antibiotics and urgent appendectomy. Follow up of patient was conducted at 5th day and 30 days 1yr. after discharge. .Outcome measures :

Primary endpoints were treatment efficacy and major complications. Efficient antibiotic treatment was defined as recovery without any need for surgery during the primary hospital stay and the 1-year follow-up should be without any recurrence. Surgical treatment was regarded as efficient based on positive findings at exploration (appendicitis or other surgical diagnosis). Negative findings at exploration were regarded as surgical failure by protocol. Secondary endpoints were minor complications, duration of hospital stay and patient experience of abdominal pain or discomfort at follow-up.

**Results :**

A total of 200 consecutive patients were hospitalized and treated due to Acute Appendicitis(between June 2014 and February 2016). Eighty percent (n = 160) received antibiotics as first-line therapy and 20% (n = 40) had primary surgery as the second line therapy. 90 %(n=144) of patients on primary antibiotics recovered while 10 % (n = 16) had subsequent appendectomy due to failed initial treatment on antibiotics within [12–48] h.18 patients (11.25%) of the 160 had experienced recurrent appendicitis at 1-year follow-up. Primary antibiotic treatment had fewer complications compared to primary surgery.

Among the 40 patients Common reasons for primary surgery were patient preference (10 patients, 25 %) and a surgeon's decision for indication of urgent operation (25 patients, 62.5 %). 3 patients have recurrent Appendicitis and 2 patients were pregnant.

Among the 40 patients who had primary surgery, 38 (95 %) had appendicitis or other surgically curable diagnoses. Thus, 5 % were negative explorations. Ninety-two percent of extirpated appendix were sent for histopathology. The proportions of phlegmonous, gangrenous, and perforated appendicitis did not differ between patients who had primary surgery and those who had rescue surgery.

Thus, treatment efficacy of acute appendicitis appeared to be 78.75% for antibiotics as the first-line therapy at one year follow up. (Table 2).

FLOW CHART OF TREATMENT
ACUTE APPENDICITIS
[N – 200]

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ANTIBIOTIC FIRST
PRIMARY SURGERY
N – 160
N – 40

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TREATMENT FAILURE -N 16 PT. RECOVERED ON ANTIBIOTICS – – 144
/
AFTER 1 YR. FOLLOW UP ( REC. APPENDICITIS & SEC. SURGERY)N – 18 (11.25%)
/
ONE YEAR ANTIBIOTIC THERAPY SUCCESS -N -126 (78%)

**Basic characteristic of patients in this trial (table-1)**

| | | SURGICAL GR. (N -40) | SURGICAL GR. (N -40) |
|---|---|---|---|
| SEX | MALE | 26 | 100 |
| | FEMALE | 14 | 60 |
| AGE (MEDIAN) | | 36 (15- 55) | 44 (16 -68) |
| VAS of PAIN | | 6 (5 - 7) | 5 (4 -6) |
| CRP (MEDIAN) | | 36 (31 – 61) | 29 (11- 63) |
| LECOCYTE COUNT (mean SD*/cmm | | 13.0 | 11.8 |
| CREATININE (med SD. mg/dl | | 1.2 | 1.1 |
| ALVARADO SCORE (MEDIAN) | | 7 (6-8) | 6 (5-7) |

VAS = Visual Analogue Scale Score Range of Pain (0-10)

**Discussion:**

The results of the present study show that the modern treatment of acute appendicitis needs change in approach. Previous randomized controlled studies have indicated that a majority of patients with acute appendicitis will heal with antibiotic treatment without the need for surgery, although such studies have displayed various kinds of scientific limitations due to unavoidable ethical considerations in protocol design .20,21,21 The most recent randomized controlled study was based on short-term surrogate markers for clinical outcome within 30 days of primary treatment. Its relevance for clinical outcome is therefore difficult to evaluate. Besides, those patients were treated with a combination of Amoxicillin and Clavulanic acid, which are usually regarded less than ideal for gastrointestinal infections.

It may be regarded as a disadvantage that not all our patients had a CT or US examination, although imaging procedures are neither completely inclusive nor exclusive for diagnosis of early appendicitis, which should be the most preferred status to treat by antibiotics in a first-line algorithm. The alternative, to compare the efficiency of Antibiotics only in patients with clear-cut signs of appendicitis on CT, relates to a different clinical question than our present protocol with treatment of unselected patients with clinically assumed appendicitis, including comparatively early appendix inflammation. Of course, this approach may imply some unnecessary antibiotics treatment due to bias inclusion of patients with nonspecific abdominal pain. However, this drawback should not be important when patients with increased CRP are treated, indicating a very high probability of any kind of abdominal bacterial infection or tissue damage where bacterial complications may be subsequent. In our present and also in previous studies, greater than 97 % of all patients with Acute Appendicitis had elevated serum CRP,9 , always indicating some kind of cellular infection/inflammation and usually not of viral origin. Our present results agree with those of most randomized studies, i.e., a majority of patients will recover on antibiotics as the first-line therapy 10.Thus, in the present study 90 % of all patients with presumed acute appendicitis, based on overall clinical criteria.

**Secondary outcome in this study (table-2)**

| | Surgical gr. (N-40) | Antibiotic gr.(n-160) | P Value |
|---|---|---|---|
| Overall complication rate% | 12.5 | 8.5 | <0.01 |
| Surgical site Infection | | | |
| Deep Incisional | 2 | NA | |
| Superficial | 5 | 1 | |
| Incisional Hernia | 1 | NA | |
| Length of primary hospital Stay (Median days) | 3.0 (2-3) | 3.0(2-4) | <0.01 |

recovered initially, and among them 87.75 % patients remained without relapse at 1 year of follow-up. It is likely that the same success should be observed for those patients who chose primary appendectomy. It remains to be confirmed what the relapse will be after 5, 10, and 30 years of follow-up.

It is important to emphasize that major complications did not differ significantly between patients who received primary antibiotics and those who were recommended for or chose primary surgery. Also, there was no difference in major complications between patients who recovered successfully on primary antibiotics treatment and those who experienced subsequent rescue appendectomy. Interestingly, minor complications were more common among patients who had primary surgery compared to patients treated with primary antibiotics, and the proportion of patients who experienced some kind of abdominal discomfort between 6 and 12 months did not differ between the antibiotic and surgical groups. Surprisingly, almost 30 % of all patients had some kind of abdominal symptom at the 12-month follow-up irrespective of their treatment schedule, which agrees with observations by others. Also, it is important to emphasize that patients treated with antibiotics as first-line therapy were not exposed to more intravenous antibiotics than patients who had appendectomy.

## CONCLUSION

In this era of technological advancement in imaging and laboratory investigations and availability of effective antibiotic, treatment protocol for acute Appendicitis should be revised Antibiotic first approach should be given a chance in selected groups and should be properly evaluated.

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